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RABIES.

A REVIEW OF RECENT ARTICLES. XVIII.*

i. *Virus.*

KRAUS and DURAN[1] in continuation of their communication on " mal de caderas " in South America, summarize the work of PATTO, HURST and PAWAN, REHAAG, and CARINI, etc. These have already been discussed in this *Bulletin*, Vol. 29, pp. 595–597. They suggest that a better name than " mal de caderas " would be " South American lyssa in cattle."

In a second communication[2] they deal more fully with the results of their examination of the Trinidad virus of HURST and PAWAN. In their experience the paralysis induced in rabbits is not characteristic of street virus rabies. It commences invariably with affection of the fore extremities, and is followed by trismus, exaggerated reflexes, paralysis and death in one or two days. The clinical picture in guineapigs is similarly unusual. A kerato-conjunctivitis with oxyphil inclusions is also a feature of inoculation with the Trinidad virus. This has not previously been observed by the authors in the case of street virus, fixed virus, Sassari virus, South American cattle virus, or the virus of "chien fou." For these reasons the authors are dissatisfied with the evidence supporting the identity of the Trinidad strain with rabies virus. A definite decision must rest upon a quantitative rather than a qualitative basis, as it is well known that close biological relationships exist between the various types of filtrable viruses. Until stronger evidence is available the authors prefer to consider the Trinidad disease as a variety of rabies (Paralyssa).

* For the seventeenth of this series see Vol. 29, pp. 595–608.

[1] KRAUS (R.) & DURAN (A.). Nachtrag zur Arbeit ueber die in Südamerika vorkommenden Epidemien der Hundswut bei Rindern und Pferden.—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1932. Vol. 75. No. 3/4. pp. 363–365.

[2] KRAUS (R.) & DURAN (Agustin). Ueber Varietäten der Lyssa. Ueber eine besondere Form der Hundswut beim Menschen auf der Insel Trinidad und ueber die Zugehörigkeit zur klassischen Form der Lyssa. II. Mitteilung. —*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1932. Vol. 76. No. 3/4. pp. 285–296. With 8 text figs. & 1 coloured fig. on plate facing p. 354.

In continuation of their former work (this *Bulletin*, Vol. 24, p. 760) LEVADITI, SCHOEN, and MEZGER[3] put forward further evidence in favour of the view that the virus of rabies is an organism of the microsporidion type (*Glugea lyssae*)*. They state that in rabid mice the development of the virus may either be (1) by grouping—in which case the initial free granulations coalesce to form plaques (Negri bodies)—or (2) by dispersion—in which case the neurones become filled with round, oval, or piriform corpuscles. They believe that the diverse oxyphil formations observed in these experimentally infected mice are specific, are intimately related to the multiplication of the virus in the nerve cell, and that they represent the almost ultra microscopic spores of *Glugea lyssae*. From experiments of which the results are given in the form of diagrammatic tables they conclude that the pathogenic activity of the brain is zero or very feeble if oxyphil formations are absent, and that, as the formations augment in quantity and in volume, the degree of virulence increases.

As the result of further histological study LEVADITI[4] concludes that the oxyphil formations found in the spaces between the Nissl corpuscles, are not related to mitochondria. The staining reactions of the two formations are quite different. They believe that the formations are colonies of rabies "germs" developed in contact with chondria, or in the canaliculi of the vacuole system.

A further communication by the same authors[5] deals with differences in the cycle of evolution of rabies virus of different strains. In some, "grouping" (see above) predominates, in others "dispersion" is the more marked. These differences depend upon the strain of virus, the species of animal inoculated, and the type of neurone affected. They also confirm the conclusion reported in the former paragraph, that though one cannot identify the rabies corpuscles (elementary or cystic) with the mitochondrial apparatus, nor with the vacuole system of the neurones, yet their results appear to show that "the units of the rabies germ multiply in contact with the chondria which serve as a culture medium and become modified in staining affinities." The variation in number or character of chondria in different neurones, and in different species of animals explains the differences referred to above.

In a fourth paper[6] they refer to their previous conclusion (this *Bulletin*, Vol. 24, p. 760) that fixed virus is a mutation of *Glugea lyssae* characterized by the loss of the faculty of the microsporidion to accomplish the pansporoblastic phase of its cycle of evolution (the Negri body). Experiments on dogs and on monkeys lead them to the conclusion that this mutation is irreversible, or at least "difficultly reversible."

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* Erroneously described in this *Bulletin* as *Glygea lyssae*.

[3] LEVADITI (C.), SCHOEN (R.) & MEZGER (J. G.). Etude morphologique du virus rabique.—*Bull. Acad. Méd.* 1932. June 7. 96th Year. 3rd Ser. Vol. 107. No. 22. pp. 782–793. With 8 text figs. [Refs. in footnotes.]

[4] LEVADITI (C.). Recherches sur la morphologie du virus rabique.—*C. R. Soc. Biol.* 1932. July 11. Vol. 110. No. 24. pp. 771–772.

[5] LEVADITI (C.), SCHOEN (R.) & MEZGER (J. G.). Morphologie du virus rabique. —*C. R. Soc. Biol.* 1932. Aug. 12. Vol. 110. No. 28. pp. 1215–1216.

[6] LEVADITI (C.), SCHOEN (R.) & MEZGER (J. G.). L'irréversibilité de la mutation du virus rabique des rues en virus fixe.—*C. R. Soc. Biol.* 1932. June 3. Vol. 110. No. 19. pp. 274–277. With 2 text figs.

In an article which should be studied by all interested in the pathological aspects of rabies, MARINESCO and STROESCO[7] examine the problems of the transmission of neurotropic ultra viruses (in particular that of rabies) and the nature of the pathological appearances in the nervous system. While not denying transmission along the axis cylinder, they favour the view that transmission is along the lymphatic spaces. Transmission depends upon various factors, "odogenesis," (*i.e.*, perivascular cell infiltration), the pH of the tissues, and differences in the potential of oxydo-reduction. These factors account for the peculiar characteristics of the various viruses—their cyto- and karyotropism—and bring about by their interaction the lesions observed in the nerve cells, and Negri bodies. The oxydase ferments of the cells of the spinal ganglia are destroyed in part, their nuclei degenerate as a result of the alteration in their catalysts, and in them no Negri bodies are found. They believe that the latter arise as the result of an "exciting" action of the virus on the nucleoli which causes the production of oxyphil granulations, which, under electro-chemical influences, traverse the nuclear membrane, and give rise to the characteristic appearances of the corpuscles of Negri thus supporting the view of ACTON and HARVEY (*Parasitology*, 1911, Vol. 4, page 255). The oxyphil substance imprisons the virus, and is essentially a rampart of cytoplasm which protects the cell against the noxious action of the ultra virus. They believe that the Negri body, which does not contain chromatin, cannot be regarded as protozoal in character since in the structure of true parasites of this type the reactions of Fuelgen and of Macallum, which demonstrate nuclear origin by detecting the presence of thymo nucleic acid, are always positive, whereas in the case of Negri bodies they are invariably negative. They conclude that the corpuscles of Negri cannot be regarded as the visible pansporoblastic phase of rabies.

A conclusion against protozoal origin is also reached by COVELL and DANKS[8]. From examination by dark field illumination of Negri bodies in the living state they find no evidence of a limiting membrane, nor of granular movements. Macallum, Fuelgen, and Millon reactions in their hands were variable and were less in favour of protozoal origin than of the origin of the inner bodies from extruded basophilic nuclear chromatin and Nissl substance. The contention that the bodies arise from constituents already present in the nerve cell as a result of the action of the virus is in agreement with their findings, but they consider the evidence for the participation of mitochondria, neurofibrils and nucleolus as inconclusive. "Both the Negri bodies and the smaller atypical lyssa bodies are probably formed by alterations in the basophilic Nissl substance, the fundamental ground substance of the cell, and by addition of variable amounts of basophilic material of nuclear origin. There is no evidence that organisms on the borderline of microscopic visibility are cloaked with these cellular components in accordance with the chlamydozoal hypothesis."

[Until the results of the Fuelgen and Macallum reactions are definitely established the question must remain in suspense.]

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[7] MARINESCO (G.) & STROESCO (G.). Études sur la pathologie de la rage.—*Arch. Roumaines Path. Expérim. et Microbiol.* Paris. 1931. Sept.–Dec. Vol. 4. No. 3/4. pp. 243–288. With 32 coloured figs. on 1 folding plate.

[8] COVELL (W. P.) & DANKS (W. B. C.). Studies on the Nature of the Negri Body.—*Amer. Jl. Path.* 1932. Sept. Vol. 8. No. 5. pp. 557–572. With 8 figs. on 2 plates. [23 refs.]

JONNESCO[9] has carried to a further stage his researches on rabies in the hedgehog. He finds that during hibernation its resistance to the virus is very high, that injections with fixed virus produce Negri bodies if the incubation period is longer than 8 days, and that these persist from passage to passage. He has observed two cases in which Negri bodies were present, but the disease could not be transmitted to rabbits—"infection mortelle auto-sterisable." When fixed virus from the hedgehog is inoculated into dogs or rabbits, Negri bodies are found, but these disappear after 3 to 5 successive passages. He believes that fixed virus inoculated into hedgehogs, acquires, in part, the character of street virus, showing that the mutation of street virus into fixed virus is not absolutely irreversible.

NICOLAU, MATHIS and CONSTANTINESCO[10] discuss in greater detail the effect of subpassage on a strain of virus of Oulou-Fato (this *Bulletin*, Vol. 29, p. 597).

A strain of street virus of exalted virulence is described by JONNESCO.[11,12] It originated from a Rumanian wolf, and in its first 19 passages through rabbits caused rabies with a constant incubation period of 3 days, followed by paralytic symptoms which resulted in death in from 1 to 3 days. Negri bodies could not be found in the brains of any of the rabbits inoculated. In the guineapig the incubation period was 2 days. The strain, when inoculated subcutaneously into 20 white mice, produced paralysis in 17 instances in 3 days, in two instances in 4 days, and in one instance in 7 days. In 12 dogs inoculated serially by the subdural route, paralysis developed in 2 or 3 days. In the brain of the dog of the eighth passage a few Negri bodies were found. Three young cocks were infected, showing paralysis on the 16th, 17th and 19th days respectively. In their brains a few Negri bodies were found. Crossed immunity experiments proved that the virus was one of true rabies.

The characteristics of the strain of fixed virus in use at Tunis have been examined by BALOZET.[13] The strain emanated from Paris and is now in its 1350th passage. The period in the case of rabbits from time of inoculation to time of death has fallen from 12 days in 1902, to $5\frac{3}{4}$ days in 1931, whilst the incubation period has fallen from 7 days to $4\frac{1}{2}$ days. The strain has also become more sensitive to desiccation; whilst the Paris virus loses virulence after 6 or 7 days, that of Tunis loses virulence in 3 days. The strain has not, however, lost pathogenicity.

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[9] JONNESCO (Demetre). Recherches sur la réversibilité du virus rabique fixe.—*Ann. Inst. Pasteur.* 1932. June. Vol. 48. No. 6. pp. 735–743.

[10] NICOLAU (S.), MATHIS (C.) & CONSTANTINESCO (Val.). Sur la transformation en virus fixe d'une souche particulière de virus rabique des rues.—*C. R. Soc. Biol.* 1932. June 17. Vol. 110. No. 21. pp. 433–435. With 2 text figs.

[11] JONNESCO (Démètre). Sur un virus rabique des rues à virulence renforcée.—*Bull. Acad. Méd.* 1932. May 24. 96th Year. 3rd Ser. Vol. 107. No. 20. pp. 688–689.

[12] JONNESCO (Démètre). Recherches sur un virus rabique de rue à virulence renforcée.—*Ann. Inst. Pasteur.* 1932. Oct. Vol. 49. No. 4. pp. 435–444. [16 refs.]

[13] BALOZET (L.). Le virus rabique fixe de l'Institut Pasteur de Tunis ; évolution et état actuel.—*Arch. Inst. Pasteur de Tunis.* 1932. July. Vol. 21. No. 1. pp. 130–143. With 1 chart. [15 refs.]

REMLINGER and BAILLY[14] from an examination of statistics of animal inoculation conclude that the virus of rabies as it occurs in Morocco does not differ in any way from that of western Europe.

ii. *Symptomatology.*

FETHERSTON and COOPER[15] relate the case of a man, bitten on the hand, who developed rabies after a month. He had not been treated, and on his demise 7 other men bitten on the hands by the same dog presented themselves for treatment. One of these died on the next day, two days later a second developed symptoms, and again two days later a third contracted the disease. In all four cases the diagnosis was established by the presence of Negri bodies. Thus four out of the eight contracted rabies, although in no case was there severe wounding. The incubation periods were approximately 29, 30, 32 and 34 days.

iii. *Diagnosis.*

It has for long been believed that intravenous injection is not a satisfactory method of experimental infection. JOWELEW (this *Bulletin*, Vol. 28, p. 746) stated that positive results could be obtained when the haemato-encephalic barrier was broken down by lumbar puncture and pumping. SCHWEINBURG[16] from an exhaustive experimental study finds that this is not necessary in the case of guineapig infection. He has succeeded in infecting 90 per cent. of these by inoculating sufficiently large quantities of a rather thick emulsion freed by filtration from the larger sized particles. A large dose is necessary, as histological examination shows that much of the emulsion is trapped in the vessels of the lung. He believes that the doses used by JOWELEW were too small, and recommends doses of 6 cc. per kilo. Intravenous infection following this procedure is as certain as intramuscular, but not so certain as cerebral, subdural or intraocular administration.

iv. *Pathology.*

The presence of rabies virus in the lachrymal gland has been investigated by TSCHESCHKOW.[17] In the case of 10 dogs infected experimentally with street virus a positive result was observed in 9 instances. In 4 out of 10 passage rabbits (fixed virus) a positive result was obtained, and in 3 out of 3 fatal human cases inoculation of an emulsion of the gland into rabbits caused rabies.

In accordance with the view of MANOUÈLIAN and VIALA that the infectivity of secretions from glands depends upon the presence of nerve cells shed into them, it is reasonable to expect that the milk of infected animals would on occasion prove infective. REMLINGER and BAILLY[18]

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[14] REMLINGER (P.) & BAILLY (J.). La rage et le virus rabique au Maroc.—*Arch. Inst. Pasteur d'Algérie.* 1932. Sept. Vol. 10. No. 3. pp. 429–435.

[15] FETHERSTON (J. E.) & COOPER (George F.). Rabies. Report of Four Deaths resulting from Bites on the Fingers by the Same Rabid Animal.—*U. S. Nav. Med. Bull.* 1932. July. Vol. 30. No. 3. pp. 314–321.

[16] SCHWEINBURG (Fritz). Versuche ueber intravenöse Lyssainfektion.—*Zent. f. Bakt.* I. Abt. Orig. 1932. June 10. Vol. 124. No. 7/8. pp. 426–453. [28 refs.]

[17] TSCHESCHKOW (A. M.). Ueber die Bedingungen des Eindringens von Tollwutvirus in die Tränendrüsen.—*Ztschr. f. d. Gesamte Experim. Med.* 1931. Vol. 78. pp. 142–146. [10 refs.]

[18] REMLINGER (P.) & BAILLY (J.). Contribution à l'étude du passage du virus rabique dans le lait.—*C. R. Soc. Biol.* 1932. June 3. Vol. 110. No. 19. pp. 239–241.

have put this to the test in the case of 7 guineapigs, 4 cats, and one dog. Inoculations were carried out 4 times with gland tissue, and 39 times with milk. Two positive results have been obtained, one with an emulsion of gland and the other with milk.

PLANTUREUX and HILBERT[19] report a case in which they believe that transmission took place through the placenta. A pup developed rabies 19 days after its birth from a bitch which died of rabies on the day of parturition. On account of the short incubation period they think it more logical to consider that infection took place through the placenta, than from the saliva of the mother.

A research carried out in collaboration with VIALA (this *Bulletin*, Vol. 28, p. 246) has been extended by NICOLAU and KOPCIOWSKA.[20] It will be remembered that they failed to find evidence of the presence of fixed virus in the brains of rabbits which had received Pasteurian treatment. Of 54 rabbits inoculated subdurally with emulsions of the vaccinated animals four have died, and in each case subpassages have been negative. The histological changes in the vaccinated animals have already been described (*loc. cit.*, Vol. 29, p. 601). In the brains of the four passage animals which died, they observe "plaques of mononuclear meningitis," glial proliferation, mononuclear infiltration between the ganglion cells of the pyriform lobe, and evidences of chronic "perivascularity." The cause of these deaths is uncertain. They may be similar to those described by REMLINGER and BAILLY (*loc. cit.*, p. 599).

In an earlier paper (this *Bulletin*, Vol. 28, p. 745) LÖFFLER and SCHWEINBURG showed that the theory that rabies antibodies were produced in the brain as a consequence of stimulation by fixed virus which had penetrated into it, was untenable. They were of opinion that the antibodies were formed elsewhere. In the present communication[21] they present evidence indicating that the seat of origin is the reticulo-endothelial system. By blocking this system with Indian ink particles they find that blocked animals are protected to a lesser degree than unblocked controls, and that the serum of animals which have been blocked is less viricidal. For example, of 8 rabbits (blocked as above) all succumbed to a test dose of fixed virus, whilst of eight unblocked controls, two developed rabies.

v. *Methods of Treatment and Statistics.*

The second analytical review by MCKENDRICK[22] of statistics from Pasteur Institutes on the results of antirabies treatment undertaken by the Health Section of the League of Nations, at the instance of the Rabies Conference (Paris 1927), has now been published. It deals with the data regarding 67,707 treated persons, and relates mainly to the year 1929.

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[19] PLANTUREUX (E.) & HILBERT (D. N.). Au sujet d'un cas de rage chez un chiot de 19 jours.—*Arch. Inst. Pasteur d'Algérie.* 1932. Mar. Vol. 10. No. 1. p. 40.

[20] NICOLAU (S.) & KOPCIOWSKA (L.). Le virus fixe existe-t-il dans le névraxe des lapins qui subissent la vaccination antirabique ?—*C. R. Soc. Biol.* 1932. June 10. Vol. 110. No. 20. pp. 348–352. With 2 text figs.

[21] LÖFFLER (Ernst) & SCHWEINBURG (Fritz). Zur Theorie der Immunität bei Tollwut (Zweite Mitteilung).—*Virchows Arch. f. Path. Anat. u. Physiol.* 1932. Feb. 5. Vol. 283. No. 2. pp. 540–549. [30 refs.]

[22] MCKENDRICK (A. G.). A Second Analytical Review of Reports from Pasteur Institutes on the Results of Anti-Rabies Treatment.—*Quart. Bull. Health Organisation, League of Nations.* Geneva. 1932. Mar. Vol. 1. No. 1. pp. 110–141.

"The figures again bring into prominence the fact that the non-European is at a much higher degree of risk than the European. They also show that the non-European is, on the average, more severely bitten than the European; that he is more frequently bitten on the bare skin; that he does not commence treatment so early; and that the animal which bit him is more frequently rabid. It has not been possible from the figures to find any indication of the existence of a racial susceptibility to rabies.

"As in the former review, no decisive evidence has been found, apart from liability to post-vaccinal paralyses, of the superiority of any one of the various methods of treatment which have been employed. Within the European group, the differences between the death rates of the various institutes are not greater than would be expected as the result of chance variations. A similar statement is also true with regard to the non-European group, but it is not true with regard to the whole statistics embracing the two groups.

"It is, however, to be noted that the statistics as submitted indicate a probable advantage in favour of modified dilution methods of treatment as compared with the others. As pointed out earlier in this review, further analysis demonstrates the presence of factors which partly account for the figures, apart from intrinsic superiority of the method; but, when all allowance is made for these factors, there appears to remain a certain amount of evidence in favour of this method as compared with the others. It should be emphasized, however, that the validity of such a conclusion depends entirely on the assumption that no unknown circumstances of importance are operating which might influence the figures decisively in favour of the method."

[A third review is at present in the press, and in it the apparent advantage in favour of dilution methods is not confirmed.]

The proportion of accidents after treatment by dried or glycerinated cords is much lower than was found in the previous review, but is still much greater than after treatment by killed vaccines.

Statistics of treatment at Sassari by FERMI are treated separately in an appendix. During the period 1900–1907, 700 persons of whom 2 developed rabies, were treated by the dried cord method. "These two individuals [who died] were both deeply bitten on the bare skin of the head, and in both cases treatment was not commenced until the 3rd week after the bite had been inflicted. From 1907 onwards [to 1930], 3,974 persons have been treated by FERMI's sero-vaccine, and, during this period, no cases of rabies have been observed."

A comparison of the protecting power of treatment by living fixed virus, carbolized fixed virus, and etherized fixed virus on groups each consisting of 12 rabbits, has been made by STUART and KRIKORIAN.[23] Of those treated by living fixed virus 42 per cent. survived a subdural test dose; of those treated by carbolized fixed virus 42 per cent survived; of those treated by ether fixed virus 50 per cent. survived, as compared with none out of three control animals. The results are not significantly different. The rabicidal properties of the sera of animals treated by the 3 methods reached maxima in 60 days, of 1 to 16 in the case of living virus, 1 to 8 in the case of carbolized fixed virus, and 1 to 24 in the case of ether fixed virus. That is to say the

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[23] STUART (G.) & KRIKORIAN (K. S.). The Rabicidal Antibody Content of Rabbit Immune Serum as an Index of Acquired Resistance to Rabies Infection.—*Jl. Hygiene.* 1932. Oct. Vol. 32. No. 4. pp. 489–493.

relative efficacies were in the proportions 2 : 1 : 3. The authors conclude from these two sets of observations that no mathematical relationship can be established between protection and rabicidal antibody content.

In the belief that the failure of treatment by antirabic sera, even of very high titre, when given either before or at the moment of infection, may be ascribed to lack of penetration of the serum into the brain substance, LÖFFLER and SCHWEINBURG[24] have investigated the effect of breaking down the haemato-encephalic barrier by means of Theocin. (This method, due to FRÖLICH and ZAK, has been used with success in the case of tetanus and diphtheria). Eighteen rabbits were given three intravenous injections of Theocin (Theophyllin sodium acetate 3 per cent., 4 cc. per kilo. of body weight), and after half an hour 3 cc. a high titre rabicidal serum. All were protected against a subsequent infective dose of rabies virus. The effect is similar to that described by SPERANSKY (this *Bulletin*, Vol. 24, p. 764), though the procedure is different.

In a further series of experiments by removing cerebro-spinal fluid by occipital puncture and introducing rabicidal serum by the same route they were able to protect animals which had been infected a short time previously (eighteen hours after cerebral infection). These investigations are being extended, and will form the subject of a future publication.

The effect of sparteine on the virus of rabies has been investigated by REMLINGER and BAILLY.[25] In a first series of experiments the effect *in vitro* was examined. Of 20 animals inoculated with virus-sparteine mixtures, 4 developed rabies, whilst of 14 inoculated with virus alone 12 died. From experiments with mixtures variously treated they conclude that the action of sparteine is not that of an antiseptic. In a second series the action *in vivo* was studied. In these, sparteine solution was injected into animals, which received immediately thereafter a test dose of rabies virus. Of 55 animals treated with sparteine 29 died of rabies, whilst of 34 control animals 33 developed rabies. It was also shown that the protection conferred was proportional to the quantity of sparteine administered, but that the site of infection—into brain, or into subcutaneous tissue—had no influence. It appeared from these experiments that the guineapig is the most suitable animal to bring into evidence the phylactic action of sparteine.

In a second paper REMLINGER and BAILLY[26] show that the inoculation of sparteine after the rabies virus had been introduced had no phylactic action, and consequently that the phylactic (or neutralizing) action of sparteine cannot be applied to the treatment of rabies.

On the analogy that chloroform is stated to have the effect of promoting the action of anti-tetanic serum by weakening the hold of the toxins on the lipoids of the nerve cell and thus facilitating the combination between toxin and antitoxin, KING[27] suggests that the action of

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[24] LÖFFLER (Ernst) & SCHWEINBURG (Fritz). Rabicides Serum im Tierversuch. —*Wien. Klin. Woch.* 1932. June 24. Vol. 45. No. 26. pp. 813–814.

[25] REMLINGER (P.) & BAILLY (J.). Phylaxie et virus rabique.—*C. R. Soc. Biol.* 1932. May 27. Vol. 110. No. 18. pp. 159–161.

[26] REMLINGER (P.) & BAILLY (J.). La spartéine inoculée après le virus rabique n'exerce aucune action phylactique.—*C. R. Soc. Biol.* 1932. July 1. Vol. 110. No. 23. pp. 674–676.

[27] KING (H. H.). The Treatment of Hydrophobia. [Correspondence.]—*Indian Med. Gaz.* 1932. June. Vol. 67. No. 6. pp. 357–358.

antirabic sera in conjunction with chloroform administration should be investigated.

REPETTO[28] reports that antirabic treatment is now carried out in the case of " numerous " persons bitten by suspected animals at Leopoldville (Belgian Congo) by the method of Fermi. (See also this *Bulletin*, Vol. 22, p. 703).

Antirabic treatment was commenced in South Carolina in 1909. SMITH[29] reports that during the period from July 1909 to October 1931, 13,849 persons have been treated, of whom 27 died of rabies. From 1909 to 1927 the dried cord method was employed in the case of 651 patients of whom 11 died (mortality rate 0·66 per cent.). From 1917 to 1922, phenolized dilutions (suspension of 1 in 1,000, in 0·5 phenolized salt solution : 21 doses of 2·5 cc.) were administered to 6,988 persons, of whom 15 died (mortality rate 0·21 per cent.). From 1927 to 1931 stronger dilutions (1 in 500 in 0·3 phenolized salt solution in the same dosage) were given to 4,738 patients of whom only 1 died (mortality rate 0·021 per cent.). No paralytic accidents have been observed throughout the 3 periods.

OUCHAKOV[30] reports that during the year 1931, 1,241 persons were treated at Leningrad, of whom one developed rabies (0·1 per cent.). The vaccine employed was that of Fermi. 2,283 persons were treated at out-stations of whom 4 died (0·2 per cent.).

From Calcutta NICHOLAS[31] reports that during the year 1930, 6,958 persons were treated of whom 42 died (0·61 per cent.). 294 of these were European and amongst these no deaths occurred. Of the Indians who numbered 6,664, 42 died (0·63 per cent.). It is stated that completed health returns were received in respect of 78·3 per cent. of those treated.

MURAT[32] from figures relating to persons treated in Algiers from 1894 to date, states that of 48,018 persons 188 died, that is a mortality rate of 0·39 per cent. When these are subdivided into race groups it appears that of 32,519 Europeans 71 died (0·22 per cent.) whereas of 15,499 of indigenous birth 117 died (0·75 per cent.).

vi. *Rabies in Animals.*

REMLINGER and BAILLY[33] have already shown that the virus of rabies may persist in the brain of the tortoise (*Testudo mauritanica*) for a period of 302 days (this *Bulletin*, Vol. 29, p. 194). They now find,

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[28] REPETTO (R.). A propos de l'existence de la rage au Congo Belge.—*Ann. Soc. Belge de Méd. Trop.* 1932. June 30. Vol. 12. No. 2. pp. 147–151. [15 refs.]

[29] SMITH (H. M.). Experience with Rabies and its Preventive Treatment in South Carolina.—*Southern Med. Jl.* 1932. Aug. Vol. 25. No. 8. pp. 876–879.

[30] OUCHAKOV (V.). Rapport annuel par l'année 1931. Service antirabique de l'Institut de Médecine Expérimentale (Léningrad).—*Arch. Sci. Biol.* 1932. Vol. 32. No. 4. [In Russian pp. 251–261. French summary p. 262.]

[31] CALCUTTA. Seventh Annual Report of the Pasteur Institute, Calcutta, for the Year 1930 [NICHOLAS (M. J.), Superintendent].—29 pp. 1932. Calcutta : Bengal Secretariat Book Depot. [8 annas ; 9d.]

[32] MURAT (H.). De la rage en milieu indigène et en milieu européen en Algérie.—*Arch. Inst. Pasteur d'Algérie.* 1932. Sept. Vol. 10. No. 3. pp. 436–437.

[33] REMLINGER (P.) & BAILLY (J.). Sur la longue persistance du virus rabique dans l'encéphale de la tortue d'eau douce (*Clemmys leprosa*).—*C. R. Soc. Biol.* 1932. June 17. Vol. 110. No. 21. pp. 421–423.

from experiments on 12 fresh water tortoises (*Clemmys leprosa*), a similar period of persistence of not less than 150 days. Neither species exhibits any symptom of rabies.

MEZGER[34] from two series of experiments confirms the above, and earlier results of REMLINGER and BAILLY. They have found the virus in the brain of *Testudo mauritanica* 26 days, and in *Cynixys belliana* 115 days after inoculation. They have never seen Negri bodies in the nerve cells.

GREVAL[35] has found Negri bodies in the brain of a mongoose which was suspected of rabies. He also reports a case of death from rabies in which the biting animal was presumably a mongoose. The relation of the mongoose to rabies epizootics is discussed (see also this *Bulletin* Vol. 28, pp. 742–743).

A case of rabies in a dog which exhibited symptoms of haemorrhagic gastro enteritis is related by ANANIADÈS and ANTONIADÈS.[36]

JAMES[37] describes a case of rabies in a horse in which the incubation period was estimated at more than sixteen months, whilst the course of the disease was under 36 hours.

TEBOULLE[38] describes rabies in the dog, and the methods of prevention employed in Alexandria.

RECORDS[39] reports that rabies reached the state of Nevada in 1915 by way of Southern California, and thereafter spread rapidly, constituting a menace to livestock and to the human community. Action was taken to reduce the number of predatory animals. A total of 99,183 of these has been destroyed between 1915 and 1930. The brains of 1,085 were examined, and 583 were found to be positive. The percentage of positives is on the decrease.

Ether virus, prepared according to the method of REMLINGER and BAILLY, has been used in the preventive inoculation of dogs in Tunis,[40] during a period of 6 months. A total of 304 have been inoculated, and of these four have died, one from rabies. In the latter case the fatal outcome cannot be ascribed to the vaccination, as the animal died 8 days after receiving treatment.

JONNESCO[41] repeats an observation, which has frequently been made, that street virus can be fixed by passage from dog to dog. After 12

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[34] MEZGER (J. G.). La conservation du virus rabique dans le cerveau de la tortue (*Testudo mauritanica* et *Cynixys belliana*).—*C. R. Soc. Biol.* 1932. Aug. 12. Vol. 110. No. 28. pp. 1292–1294.

[35] GREVAL (S. D. S.). Rabies in the Mongoose. (Reports from Records, including a Report on the First Positive Brain of Mongoose examined at Kasauli. Comments including Speculation and Bearing on Treatment.)—*Indian Med. Gaz.* 1932. Aug. Vol. 67. No. 8. pp. 451–453.

[36] ANANIADÈS (B.) & ANTONIADÈS (C.). Syndrome gastro-intestinal de la rage chez un chien.—*Rev. Gén. de. Méd. Vet.* 1932. June 15. Vol. 41. No. 486. pp. 331–332.

[37] JAMES (Allan J.). An Atypical Case of Rabies.—*West African Med. Jl.* 1932. Apr. Vol. 5. No. 4. p. 70.

[38] TEBOULLE. La rage chez le chien.—*Rev. Prat. Malad. des Pays Chauds.* 1932. Feb. 11th Year. Vol. 12. No. 2. pp. 55–59.

[39] RECORDS (Edward). Rabies—its History in Nevada.—*California & Western Med.* 1932. Aug. Vol. 37. No. 2. pp. 90–94.

[40] BALOZET (L.). Les six premiers mois d'application de la vaccination antirabique des animaux à l'Institut Pasteur de Tunis.—*Arch. Inst. Pasteur de Tunis.* 1932. July. Vol. 21. No. 1. pp. 176–180.

[41] JONNESCO (Demetre). Recherches sur la vaccination préventive des chiens avec le virus rabique fixe-chien.—*Ann. Inst. Pasteur.* 1932. Sept. Vol. 49. No. 3. pp. 332–342.

sub-passages Negri bodies had disappeared, and after 85 passages the incubation period became fixed at 7 days. This dog fixed virus is effective in the immunization of dogs and is said to be superior to rabbit fixed virus.

vii. *Postvaccinal Paralysis.*

TARTAKOFF and VIBBER[42] discuss two cases of postvaccinal paralysis following treatment by Semple's method. Neither was fatal. In the first the symptoms were those of a dorso-lumbar myelitis, the second was of the Landry type.

viii. *Miscellaneous.*

In 1897 DELÉARDE published the statement that animals alcoholized during the course of vaccination do not acquire any immunity against rabies. REMLINGER and BAILLY[43] as the result of experiments upon 20 rabbits, show that the rabicidal power of the serum of alcoholized animals is identical with that of animals which have received no alcohol. Though they will continue to recommend abstinence during the course of antirabic treatment, there is no evidence that non-adherence leads to the failure of the treatment.

From experiments on rabbits NICOLAU, CRUVEILHIER and KOPCIOWSKA[44] find that injection of fixed virus brain administered before (14 rabbits), during (16 rabbits), or after (9 rabbits) the injection of sheep red blood cells, augments the titre of haemolysins in the serum to a much greater degree than does the injection of emulsions of normal brain. Thus where the blood cells were introduced first, the titre in the case of fixed virus brain rose to a maximum of 6,000, in the case of normal brain it rose to about 2,250, and in the controls, which had received no brain substance of either sort, to about 750.

A. G. McKendrick.

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[42] TARTAKOFF (Joseph) & VIBBER (Foster L.). Rabies Vaccine Encephalomyelitis. Case Reports.—*New England Jl. of Med.* 1932. Sept. 15. Vol. 207. No. 11. pp. 497–498.

[43] REMLINGER (P.) & BAILLY (J.). L'alcoolisme expérimental ne s'oppose pas à l'établissement de l'immunité antirabique.—*Bull. Acad. Méd.* 1932. May 31. 96th Year. 3rd Ser. Vol. 107. No. 21. pp. 734–737.

[44] NICOLAU (S.), CRUVEILHIER (L.) & KOPCIOWSKA (L.). Influence de la vaccination antirabique sur l'élaboration des hémolysines dans l'organisme du lapin.—*C. R. Soc. Biol.* 1932. June 27. Vol. 110. No. 22. pp. 533–535. With 2 text figs.

PELLAGRA.

STATISTICAL BULLETIN. METROPOLITAN LIFE INSURANCE CO. 1932. June. Vol. 13. No. 6. pp. 5–7.—**Pellagra Mortality among Wage-Earners.**

The pellagra death rate in America, particularly in the Southern States, for 1930 and 1931 has declined. This is true both of the wage earning classes and of the community as a whole. It is remarkable that this should be so in view of the widespread unemployment which has prevailed, especially in 1931.

A study of pellagra mortality among Metropolitan industrial policy holders for the period 1911–1931 shows no continuous trend. The highest figures were recorded in 1914 and 1915 but after this a continued fall took place reaching its lowest in 1924. For the next five years the curve took an upward trend until recently when it has fallen again. Thus "the facts do not show that the higher mortality rates always comes when business is at a low ebb." It is probable that the distribution of brewers' yeast by health departments is responsible for the recent fall in the death rate.

As regards other factors, colour and sex play an important part. The pellagra mortality rate among negroes is from two to five times the figure for whites and there is a preponderance of females, especially in the black races. *A. D. Bigland.*

WILSON (H.). **Pellagra in Egypt.**—*Jl. Egyptian Med. Assoc.* 1932. July & Aug. Vol. 15. Nos. 7 & 8. pp. 405–426; 490–503. With 8 charts.

No reliable statistics showing the prevalence of pellagra in Egypt are to be obtained. In 1902 SANDWITH found that in many Egyptian villages 35–62 per cent. of the fellahin were affected. Applying these figures to the adult population only, it would mean that 1½–3 million persons suffered from the disease. This figure is probably too high, as in it are included cases showing slight cutaneous or alimentary disturbances which to-day would be regarded as non-pellagrous. Moreover the admissions to Kasr el Aini Hospital and to the asylums 30 years ago do not suggest that such an enormous figure was ever accurate. Thus in 1900, 82 cases of pellagra were admitted to Kasr el Aini while during the years 1919–1928 the average annual admission rate was 84. In 1915 STIVEN found 4 per cent. of the inhabitants of villages in Sharkieh and Asyut were affected. If this figure be generally true then 400,000 persons in Egypt (excluding the large towns) are sufferers.

A further study of this problem was undertaken, the material comprising (1) admissions of pellagrous insane to mental hospitals during 1916–1931. (2) Pellagra cases among persons in prisons during 1917–1931. (3) Pellagra cases admitted to P.H.D. hospitals 1919–1928. The main findings are as follows :—There is no evidence that pellagra in Egypt has increased or diminished to any marked extent during the last 30 years ; during the years 1916–1922 there was a marked increase in the disease, possibly due to low wages and the high cost of living ; the incidence rate in Lower Egypt is nearly twice that in Upper Egypt and is probably related to the type of foodstuffs cultivated.

The second part of the paper deals with the etiology of pellagra. In respect to the part played by maize, it is suggested that the low value

of maize protein compared with that of wheat and rice is an important factor. The author estimates that "a man would require in this country (Egypt) to consume not less than 2,000 grammes of dura bread a day if he were unable to supplement his diet by food of a higher protein value." The question of the possible toxic effects of maize, spoiled or unspoiled, is discussed as is also MELLANBY's finding that toxic substances (toxamins) in cereals give rise to pathological conditions and that these toxamins can be neutralized by the appropriate vitamin. Thus, according to MELLANBY, the cutaneous symptoms of pellagra are due to vitamin B_2 deficiency while the nerve lesions are caused by the presence of a toxamin more especially present in maize. Nevertheless, the work of ROSCOE shows that maize contains weight for weight the same amount of vitamin B_2 as wheat and certainly more than does rice. Furthermore, if maize were definitely toxic then the greater the amount consumed the worse should be the pellagra symptoms; most workers will agree that the opposite is the case.

Dietary deficiency and its connexion with pellagra receives full consideration. Investigation of various diets reveals that neither deficiency nor excess of carbohydrates has any association with the disease and the same is true of fats, whether animal or vegetable. There is room for further research regarding mineral constituents, especially iodine, manganese and copper. Aluminium and silica are not considered to be of etiological importance.

The author is of the opinion that whatever may be the importance of lack of vitamin B_2 in producing dermatitis in rats and black-tongue in dogs it is not the cause of human pellagra. "There is certainly no symptom in pellagra so distinct and characteristic as to really justify

TABLE VII.—Relative Value of some common Food Materials in regard to Pellagra assessed from their protein content valued on the basis of K. Thomas's original figures for the biological value of different proteins.

*A. Anti-Pellagrous value of protein of different origin.		†B. Available protein per cent. in some common foods.		§C. Quantities of some common foods of equal A.P. protein value.	
Animal Protein	100 (1·0)	Meat	19	Meat	100
Rice	88 (1·1)	Milk	4	Pulse	180
Potato	80 (1·2)	Rice	6·7	Rice	300
Pulse	55 (1·8)	Potato	1·5	Milk	470
Wheat	40 (2·5)	Pulse	19	Wheat	675
Maize & Millet	29 (3·4)	Wheat	7	Maize & Millet	1,000
		Maize	6·7	Bread. Wheat	1,000
		Millet	6·6	Maize or Millet	1,800

*A. The figures in brackets are the factors by which the net (available) protein of the different components must be divided to obtain the anti-pellagrous value.

† B. These figures represent the gross protein less the percentage normally lost from a mixed diet in the alimentary tract.

§ C. These figures are calculated from the data given in parts A. and B. of this table.

"To obtain the protein value of any given diet the protein content of each component is estimated and (after deducting 20 per cent. for loss in digestion from vegetable and 5 per cent. from animal proteins) divided by the factor corresponding to Thomas's figure for that particular type.

"The figures so obtained are added together and give the value of the protein of the whole diet in terms of animal protein."

the assertion that any pathological condition found in the lower animals is the true analogue of the human disease." Therefore, the best method of tackling the problem of pellagra is to examine the B_2 content of those diets which have been known to be associated with either the causation or cure of the disease. Tables are given showing the relative content of vitamin B_2 in various foodstuffs and the weight of common foods of equal B_2 value. It is claimed that a perusal of these figures will convince anyone that deficiency of vitamin B_2 has no connexion with pellagra. For example, 150 grams of meat added to a pellagrous diet of sufficient caloric value will cure the disease, while 210 grams of maize will not, and yet the B_2 content of each is about the same. Again, consideration of pellagra producing and preventive diets show that there is no consistent relation between the B_2 value and the incidence of the disease.

On the other hand there is a definite connexion between the protein value of the diets and pellagra. This protein value is dependent upon the amino-acid content and it is well known that vegetable proteins are less able to maintain nitrogen equilibrium than those in meat and other foods. The relative protein value of common foodstuffs is given in a chart and by calculation the "meat value" or the "antipellagrous value" of any diet can be obtained. When this figure falls below 40 grams daily the diet is pellagrous, while above this it is not, except when the protein requirement is raised by labour or in the presence of some factor which seems to exist in asylum conditions. Among other predisposing factors must be mentioned intestinal infections, such as dysentery and helminthiasis, and a previous attack of pellagra.

From a consideration of the above findings the author is of the opinion that "it seems impossible to avoid the conclusion that the cause of pellagra is a deficiency not so much in the absolute quantity as in the quality of the protein." *A. D. B.*

BOGGS (Thomas R.) & PADGET (Paul). **Pellagra. Analysis of 102 Cases.**—*Bull. Johns Hopkins Hosp.* 1932. Jan. Vol. 50. No. 1. pp. 21–32. With 2 figs. [14 refs.]

The first part of this paper is summarized in the authors' own words: "(1) an analysis of 102 cases of pellagra is presented. (2) 31 of the cases were of the simple variety; 40 were post-alcoholic; and in 31 cases the disease arose as a complication of some other malady. (3) The alcoholic variety of pellagra has become more than four times as common since the enactment of Prohibition. (4) The clinical features of the disease are pointed out, the diagnosis is discussed, and the observation is made that there exists no difference between the three types."

Treatment consisted entirely in the liver diet of Minot and Murphy. Liver extract was tried in a few cases and proved equally effective. Out of 36 uncomplicated cases treated with liver diet alone 25 recovered, 7 died and 4 had residual nervous symptoms. Out of 35 similar cases not receiving liver diet 9 recovered, 24 died and 2 had residual nervous symptoms. Moreover, in the first group of recovered cases the average hospital stay was 32 days compared with 56 days in the second group.

For the dermatitis oily and greasy preparations are to be avoided; talcum powder gives much relief. The stomatitis can be controlled by a paste of sodium perborate or a solution of potassium permanganate; local applications of neoarsphenamine are unsafe. Hydrochloric acid

in liberal doses is almost specific for the diarrhoea, and this remedy, too, may prove effective in the treatment of spinal cord changes. The psychoses are very resistant to all therapeutic measures. Blaud's pills (90–120 grains a day) or iron ammonium citrate is recommended for the anaemia. *A. D. B.*

FAKHRY (Assad). **Recent Advances in Diagnosis of Pellagra. The Utilisation of the Erythrocyte Sedimentation Rate in the Diagnosis of Pellagra. With a Demonstration of the Writer's Apparatus to record automatically the Result of the E.S.R.**—*Jl. Egyptian Med. Assoc.* 1932. July. Vol. 15. No. 7. pp. 427–437. With 1 chart & 5 figs. on 3 plates.

At the Kafr-El-Zayat Ankylostoma Hospital, Egypt, the author saw 214 cases of pellagra during 1930, and 202 during 1931. He computes that in Egypt there must be about 200,000 pellagrins. Among various clinical observations the following may be noted.—An unsuccessful attempt was made to transmit the disease by repeated injection of pellagra blood into a healthy subject. The wet type of the disease is very rare, being encountered only once in the series. Dermatitis of the fingers and toes is unusual probably owing to their protection from the sun's rays during work. Facial seborrhoea, however, was noted in 5 cases. Stomatitis is the earliest manifestation of pellagra. The incidence of intestinal bilharziasis was very high and the patients showed varying grades of anaemia, though the R.B.C. count was normal and leucocytosis was present, possibly due to the concentration of the blood following diarrhoea.

Particular attention was given to the erythrocyte sedimentation rate and an apparatus for recording this automatically is described. The reading in 10 normal cases varied from 3–10 per cent. after the first hour. In pellagra " 32 per cent. of the cases gave a reading between 10 and 30, 35 per cent. showed figures between 31–50, 27 per cent. between 51–70, and 6 per cent. above 70." " The characteristic thing about the E.S. curve in pellagra is that the corpuscles sediment rapidly in the second quarter of the first hour." *A. D. B.*

ISMAIL (Ahmed Shafick). **The Mental Aspect of Pellagra.**—*Jl. Egyptian Med. Assoc.* 1932. Aug. Vol. 15. No. 8. pp. 504–511.

According to different observers the number of pellagrins showing some form of mental trouble varies from 4 to 15 per cent. The association of pellagra with insanity is three-fold: (1) The physical disease may precipitate a latent predisposition and thus be merely the exciting cause of such conditions as manic-depressive insanity, dementia praecox, etc. (2) Pellagra may be associated with conditions such as mental defect, epilepsy, etc., especially when the patients are unable to look after themselves. (3) Pellagra may be the actual cause of the mental disturbance.

True pellagra psychosis is an intermittent and progressive amentia, which terminates in dementia if not cured. During the years 1912–1920, 757 insane pellagrins were admitted to Khanka Mental Hospital, Egypt. Of these cases 320, 42 per cent., were classified as amentia (confusional insanity), the typical psychosis of the early stages. On further analysis of the figures 81 cases of mania and 86 of melancholia were added, making the total for amentia 64·5 per cent. This series

has now been extended up to 1931 and it was found that out of 978 pellagra cases 520 could be classified as acute confusional insanity. Of the 69 admissions during the year 1912 [*sic*], 13 were discharged, 31 died and 25 who remained in hospital became demented.

In general, before admission to hospital the patient has usually been depressed and irritable for some time. When certification becomes necessary suicidal tendencies are frequently found; thus in the 978 cases 234 were definitely suicidal, and 229 doubtfully so. So common is suicide by drowning that the term "hydromania" is used by the authorities. *A. D. B.*

RASSULEV (J. A.). Ueber Diabetes insipidus bei Pellagra. [**Diabetes Insipidus in Pellagra.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1932. Sept. Vol. 36. No. 9. pp. 481–489.

The author describes three cases of a diabetes insipidus syndrome occurring during the course of pellagra. In two of the cases the pellagra symptoms were definite but in the remaining one a diagnosis of pellagra-sine-pellagra was made. The symptoms were excessive thirst and the excretion of large amounts of urine of low specific gravity. Thirst might have been due in these cases to the associated diarrhoea, but had this been so, oliguria and not polyuria would have been present and the specific gravity would have been high and not low. Radiologically there was no change in the sella turcica but injection of pituitrin gave temporary relief. The fact that improvement in the pellagra symptoms was accompanied by a retrogression of the diabètes insipidus syndrome suggests that the latter may be regarded as a true symptom of the former. The author also points out that the syndrome may be of value in the diagnosis of pellagra from other conditions which resemble it. [It is too ambitious to state after the observation of only three cases that diabetes insipidus occurs in 25 per cent. of pellagra cases.] *A. D. B.*

THAYSEN (Th. E. Hess). **Secondary Pellagra.**—*Acta Med. Scandinavica.* 1932. Vol. 78. No. 3–6. pp. 513–559. With 13 figs. [1 page of refs.]

Secondary pellagra is the term applied to that form of the disease which develops in patients suffering from chronic maladies of the digestive tract. Two such cases are described in very great detail.

The first case was that of a woman, 19 years of age, who $3\frac{1}{2}$ years previously had been under treatment for ulcerative colitis. This was followed by appendectomy and she was well until the autumn of 1930. In September 1930 she began to suffer from dyspepsia and vomiting. In January 1931 for three weeks she was fed entirely through a duodenal tube. In February diarrhoea began and in April stomatitis and skin lesions on the face and hands made their appearance. Anaemia, symptoms suggestive of combined degeneration of the cord and osteoporosis were also present. The diarrhoea was not improved by medical treatment and antipellagrous diet but Natein tablets (4×2) were very successful and rapid recovery, which was maintained, resulted. A diffuse hypertrichosis developed in this case but cleared up with the disappearance of the other symptoms.

The second case was that of a woman, aged 48, who for many years had suffered from dyspepsia, achylia and constipation alternating

with diarrhoea and associated with dilatation of the colon. "The first symptom of secondary pellagra was mental depression, developing in the course of the summer and autumn, improving in the following winter, and progressing again next spring, this time accompanied by pellagrous dermatitis, stomatitis with dysphagia, and proctitis. Aggravation of the depression and aversion for food. Death." Autopsy revealed nothing of importance except dilatation of the colon and splenic enlargement.

A very full survey of the literature of secondary pellagra is given and analysis of the cases shows that the primary digestive disturbance most frequently consists of "stenosis of the digestive alimentary canal (ca. 31 cases), chronic diarrhoea (7 cases), or diarrhoea alternating with constipation (4 cases). Gastritis with achylia or hypochylia, exclusion of gastric digestion through jejunostomy, or abnormal stomach function (pyloric stenosis) was found in 87 per cent. of the entire material."

The cause of secondary pellagra is discussed in relation to the etiological studies of GOLDBERGER. The avitaminosis in the author's first case may have been exogenous but probably was endogenous, as undoubtedly it was in the second case. *A. D. B.*

SABRY (Ibrahim). **On the Chemical Nature of the Pellagra Toxin and the Discovery of the Thiosulphate Treatment of Pellagra.**—*Jl. Egyptian Med. Assoc.* 1932. June. Vol. 15. No. 6. pp. 365–389. With 4 plates. Also in *Jl. Trop. Med. & Hyg.* 1932. June 1. Vol. 35. No. 11. pp. 164–172. With 1 fig.

BLOCH of Zurich has shown that the human pigment melanin is formed from a mother substance allied to tyrosin which he has named "dopa," by the action of a ferment, "dopa oxydase," found mostly in the basal layer of the skin. Assuming that pellagra is a toxaemia and that its chief symptom is pigmentation of the skin then the toxin must be causally related to this pigmentation. In other words, it must be dioxyphenilalanine, *i.e.*, tyrosin containing two hydroxyl groups instead of one. Thus the "dopa" of BLOCH is similar to pellagra toxin. "Dopa oxydase" ferment is stimulated and activated by the sun's rays. It is claimed, moreover, that hyper-pigmentation in pellagra is Nature's method of cure, since the "dopa" or toxin of the disease is deposited in the skin as harmless melanin.

The periodicity of pellagra is explained as follows.—Maize in Egypt is collected and dried during December and early January sees its entry into the peasants' diet. Now, the skin symptoms of the disease appear in March. During these three months "dopa," derived from maize, has been accumulating in the body and its neutralization and deposit as melanin begins. If now the patient be allowed no more "dopa" in his diet, in time all the toxin will be neutralized and recovery will take place. But patients usually continue their harmful diet after the rash has disappeared in May or June with the result that in the beginning of autumn the skin symptoms reappear. This explanation has clinical support in that autumn cases are more severe than those in spring and show a higher mortality.

The author is strongly opposed to the vitamin-deficiency theory of pellagra. He argues that the thiosulphate treatment could not cause the remarkable improvement it does if the disease were an avitaminosis, and he points out that the Egyptian peasant consumes large amounts of vitamins especially during the winter months. Every one of the author's 97 cases admitted the consumption of milk which is

known to be rich in vitamin G. The experimental condition produced in the rat by vitamin G deficiency " only in part superficially resembles some symptoms of pellagra." Cases of pellagra where no dietary defect can be discovered also strengthens the author in his belief in the toxic nature of the disease.

In order to gather further information on the role of maize in pellagra etiology the author visited villages in Upper and Lower Egypt during the maize harvest. He was struck with the multiplicity of colours found in the grain and he came to the conclusion that a pigment-forming substance similar to " dopa " was present in maize and that this had undergone oxidation. Upon such grounds he is of the opinion that maize is only etiologically important because it contains a toxic substance which may be, and is, present in other foods. Two cases of pellagra occurring after the consumption of large amounts of an artificially pigmented wine are described.

Coming to the influence of sodium thiosulphate on pellagra, experiments are described which tend to show that " dopa " in the presence of thiosulphate is chemically changed and a connexion is traced between the colour of maize grains and their toxicity. Therapeutically 10 cc. of a 10 per cent. solution of pure sodium thiosulphate in distilled water are given daily by intravenous injection. The results obtained in all the 97 cases treated were " more or less the same." The skin lesions disappear after 5–6 injections, the other symptoms shortly follow suit and " the pellagra is aborted by a course of 10–15 injections." As regards relapses it is difficult to say whether these are due to insufficient treatment or to a fresh invasion of the causal toxin. Four patients were kept under observation in hospital for a year after the date on which they would normally have been discharged and none has so far relapsed. *A. D. B.*

WHEELER (G. A.) & SEBRELL (W. H.). **The Control of Pellagra.**—*Jl. Amer. Med. Assoc.* 1932. July 9. Vol. 99. No. 2. pp. 95–98.

Etiological factors in pellagra fall naturally into two groups. The first concerns the individual and includes such conditions as food fads, alcoholism, gastro-intestinal disease and other disturbances resulting in a disordered diet. From such causes sporadic cases arise. The second group concerns the community and includes the vital factors of food supply and the money wherewith to obtain it. In this group is found endemic pellagra which accounts for perhaps more than 98 per cent. of all cases. During 1930 7,146 deaths from pellagra in the U.S.A. were recorded. Of these 97·9 per cent. occurred in those states lying wholly or partially within the cotton belt. Morbidity figures show that for each death there are not less than 35 cases of the disease and for every case there is a large number of sufferers from minor degrees of malnutrition and debility.

" In no disease is the response to proper treatment or prophylaxis more gratifying." Why then is not more progress being made in pellagra control ? It is one thing to draw up a program but quite another thing to have it carried out, especially as the ultimate responsibility falls upon the sufferers themselves. The important point is to have readily available an adequate poverty-resistant and depression-proof diet. This is difficult to obtain when farms depend upon growing cotton and become less and less self-supporting as regards other crops. Curiously enough the present slump in the price of cotton

which has brought about an increase in the prevalence of pellagra will, if continued long enough, eventually correct matters by forcing farmers to grow other crops.

In approaching the problem of pellagra control it must be remembered that about 90 per cent. of the cases have their onset during the months April–July. As it takes from three to five months of restricted diet to produce pellagra it follows that during the late winter and early spring the diet should receive particular attention. The Public Health Service has examined the pellagra-preventive power of 35 foodstuffs, and a list is given showing which are of value and which are lacking in this respect. It will be seen that during the early portion of the year the diet of many people in the pellagrous districts is limited almost entirely to the non-preventive class of foodstuffs. These foods are useful as a basis for nutrition but require supplementing.

The concluding remarks have an obvious bearing upon prophylaxis: "In looking for cases of pellagra the home surrounded by evidence of a good garden, or a cow or two, a few pigs and some poultry may as well be passed up, for the chances are less than one in a thousand that pellagra will be found. On the other hand, the home surrounded only by last year's cotton patch will always bear watching." *A. D. B.*

SANDELS (Margaret R.) & GRADY (Eunice). **Dietary Practices in Relation to the Incidence of Pellagra. I. A Study of Family Dietaries in Leon County, Florida.**—*Arch. Intern. Med.* 1932. Sept. Vol. 50. No. 3. pp. 362–372. With 1 graph. [20 refs.]

A study of the dietaries of 29 families in Leon County, Florida, is here described. In 16 of these families one or more active cases of pellagra were present (in all but one the only adult affected was the housewife). The remaining 13 families were free from the disease and served as controls. Thus dietary records, 93 in number and covering a period of 7 days each, were collected during midwinter, spring, late summer and fall.

Comparison of the records of the pellagrous and control families shows differences in the use of milk and succulent vegetables, especially during the fall and winter. The supply of lean meat and fish in the two groups was similar but there were some slight changes found in the use of eggs, cheese and fruit.

This distinct seasonal variation in the supply of milk and succulent vegetables "confirms the observations of previous investigators and extends their findings in showing that this seasonal influence is sufficiently more marked in the dietaries of the pellagrous families to constitute an important difference in the dietary practices of the two groups."

"The results would seem to justify emphasis, in practical dietary recommendations, on the need for an increased use of succulent vegetables during the months when garden produce is less plentiful and for the establishment of a uniformly liberal milk supply throughout the year." *A. D. B.*

UNDERHILL (Frank P.). **Clinical Aspects of Vitamin G Deficiency.**—*Jl. Amer. Med. Assoc.* 1932. July 9. Vol. 99. No. 2. pp. 120–124. [35 refs.]

Vitamin G is the new name given to the heat-resistant pellagra-preventive factor. The view that deficiency of this vitamin is entirely

responsible for causing pellagra must be accepted with some caution. It is possible that several deficiencies are involved.

The whole subject of pellagra etiology is reviewed from the clinical and experimental standpoint. The present position is well summed up in the words of TURNER : " It is now five years since Goldberger and his colleagues announced their studies on the value of factor P-P (now called vitamin G or B_2) in preventing the relapse of cutaneous pellagra in a group of patients in the Milledgeville Hospital. These results have been accepted widely as establishing the identity of pellagra with certain syndromes produced in experimental animals, and as final proof that factor P-P is the cause of pellagra. During these years those of us who see pellagra frequently have seen a large percentage of patients either die or go into chronic illness in spite of what appeared to be ample opportunity for vitamin therapy to have been effective. The rather poor showing of vitamin therapy in pellagra may be used either as argument against the specificity of vitamin G or it may be interpreted as indicating that changes have taken place due to pellagra or some other disease or constitutional state which makes the vitamin ineffective."

It is only fair to state that vitamin G, or indeed any therapeutic measure, may be useless when structural changes have taken place and the author points out that in his own experimental work with dogs it is much easier to prevent the appearance of symptoms than to cause their disappearance. Even so, in early stages of the experimental disease cure is obtained.

Finally there is a discussion of pellagra occurring in alimentary disorders as a secondary condition, for example in alcoholics and among wealthy patients who in spite of plentiful food for some reason, probably psychological, refuse to take a well balanced diet. ROBERTS has recorded 25 such cases in none of which was a balanced diet of meat, milk, eggs or wholesome vegetables taken. It is significant that in this group there were 21 women. The treatment of epilepsy with a ketogenic diet has led to the appearance of pellagrous symptoms and these have cleared up upon the resumption of normal feeding.

A. D. B.

BERIBERI.

MAKI (Hiroshi). Observation statistique des décès causés par le béri-béri au Japon propre. [**Deaths from Beriberi in Japan.**]—*Kitasato Arch. Experim. Med.* 1932. July. Vol. 9. No. 3. pp. 202–217. With 7 graphs.

——. Observations statistiques des décès causés par le béri-béri au Japon (non compris les colonies).—*Rev. d'Hyg. et de Méd. Préventive.* 1932. Nov. Vol. 54. No. 9. pp. 649–662. With 7 graphs. [Summary appears also in *Bulletin of Hygiene.*]

In the 10 years 1920–29 there were in Japan on the average 17,000 deaths from beriberi annually, a death rate of 29·4 per 100,000. Of these, 62 per cent. were deaths of males, 38 per cent. of females ; this sex discrepancy is at its maximum at ages 45 to 70 when 84 per cent. of the deaths relate to males. At ages 0–4 there is very little difference between the sexes, but at ages of adolescence males are also specially affected. The death rate is at its highest in the first year of life, 416 per 100,000, becomes negligible at ages 2–9, rise to about 25 per 100,000 at ages 20–24, and is about 11 to 13 per 100,000 at ages 40–80. The deaths show a marked seasonal distribution, rising in May and reaching their peak in the autumn. In fatal cases three-quarters of the deaths follow an illness of less than one month. The death rate of the large towns is more than twice that of the rural areas and small towns. Amongst infants the greatest number of deaths falls in the second month of life, and thereafter falls progressively. Beriberi is shown by these statistics to be one of the important causes of death in Japan, especially as a cause of infant mortality. *A. Bradford Hill.*

PARREIRAS (Decio), ALTINO DE ARAUJO (Edgar), RAMOS (Mario), GONÇALVES (Barreto), BARROS (Ruy Rego), LUCENA (J.) & DE OLIVEIRA (Luciano). Contribuição ao estudo do beriberi. [**Contribution to the Study of Beriberi.**]—75 pp. Departamento de Saúde Publica. Estado de Pernambuco. (Publicação N.3). 1932. Aug. [Summary appears also in *Bulletin of Hygiene.*]

When, in December 1931, cases of a disease which appeared to be assuming an epidemic character occurred on the island of Fernando de Noronha, off the coast of Brazil, information was sent to the Director of the Department of Public Health of the State of Pernambuco and a commission of experts was deputed to investigate it. This publication gives an account of the enquiry and its results ; it is divided into six chapters each written by a different member of the commission. All agreed that the disease was beriberi.

Chapter I, by Dr. Gonçalves, describes the geography of the island, its situation, constitution, climate, the inhabitants and the dwellings they occupy ; he gives also analyses of the water supply. The island serves as a penal settlement, for both civil and military offenders, and the inhabitants consist largely of prisoners and those engaged in looking after them. In chapter II Dr. Parreiras discusses the epidemiology of the outbreak which began in December 1931, reached its acme in the following April and died down rapidly from May onwards. The constituents of the food ration are given, and appear to be in quantity adequate, but nothing is said as to the mode of preparation.

The total population was 1,560 and among them were 135 cases ; in successive months from December to May the numbers attacked

were 3, 17, 23, 24, 57, 11. 131 cases occurred among 1,306 males (10 per cent.) and only 4 among 254 females (1·6 per cent.). The age incidence is also given in a table showing that more than half, 78 out of 135, were between 21 and 30 years, but as the numbers at the different ages are not stated these figures convey no information of value. There were 11 deaths. In a former similar outbreak in 1919 there were 8 fatal cases [the number then attacked is not stated]. A most noteworthy point is that the incidence among the soldiers who were better fed and housed was 104 among 357 (29 per cent.) and among 615 prisoners only 20 cases (3·2 per cent.).

Dr. Ramos, in the succeeding chapter, describes his laboratory investigations on the kakke bacillus of Matsumura. He carried out more than 6,000 agglutination tests and identified the organism, *Bact. coli communius*, in 25 of 36 stools examined (69 per cent.) and agglutinated it with the serum of patients, but, on the other hand, 25 sera out of 50 normal, healthy subjects (50 per cent.) also agglutinated it and he draws the natural conclusion that this organism is not specific of beriberi.

Dr. Barros studied the basal metabolism of 11 patients and found it high in all, contrary to what is usually the case in beriberi.

In chapter V Dr. Altino de Araujo gives an account of the clinical aspect, the chief symptoms being general weakness, especially marked in the legs, oedema of legs, palpitation and dyspnoea, with rapid death in some patients. A few suffered from gastro-intestinal disturbance, nausea, vomiting and diarrhoea, early in the illness. The blood pressure findings are interesting. Of 54 patients examined 34 had a normal maximum, 29 a normal minimum [presumably by maximum and minimum is meant systolic and diastolic pressures] ; 16 had a maximum and 2 a minimum above normal and 4 a maximum and 23 a minimum below normal. In other words the maximum was normal in 63 per cent., raised in 30, lowered in 7, while the minimum was normal in 54, raised in 4 and lowered in 42 per cent.

In the final chapter Dr. Lucena speaks of the nervous symptoms present and the results of examination of the cerebrospinal fluid by the Lange test and the Wassermann reaction. Six showed a definite disturbance of tactile sense with zones of hyper- and hypo-aesthesia ; in 2 patients there was allocheiria, 5 had paresis or actual paralysis, 18 complained of pain on pressure of the calf muscles and passive movement was also painful ; the knee jerks were abolished on both sides in 7, unilaterally in 1, diminished in 6, brisk in 5, normal in the rest. The calf muscles were atrophied in 8, and in 3 the thenar and hypothenar muscles. The ocular reflexes were unaffected. *H. H. S.*

HILLERET & CHARPENTIER. Considérations médico-militaires sur quelques cas de béribéri constatés au ler bataillon sénégalais de Tananarive et au 2e bataillon malgache de Majunga du ler régiment mixte de Madagascar. [**Beriberi in Native Troops in Madagascar.**]—*Ann. de Méd. et de Pharm. Colon.* 1932. Jan.–Feb.–Mar. Vol. 30. No. 1. pp. 90–95.

During December 1930 a small outbreak of beriberi occurred in a battalion of French Colonial Troops at Antananarivo, Madagascar. Of 20 cases showing oedema of the legs 2 proved to be suffering from old cardiac lesions, 10 had ankylostomiasis but the remainder were apparently true cases of beriberi. Measures such as giving " red "

rice ; partial substitution of European food for native diet ; the consumption of meat, fish, potatoes, tomatoes, fresh fruit, etc., and the reduction of physical fatigue to a minimum soon proved successful.

In another battalion at Majunga a second outbreak occurred during April 1931. Of the 16 cases 4 were serious and 1 died of acute myocardial weakness. Prophylactic measures were put into operation and by June no fresh cases were reported.

Apparently the cause of these two small epidemics was the eating of imported rice, the milling of which had been too complete and performed too long a time before consumption. *A. D. Bigland.*

BELMONTE (Demetrio). **Preliminary Studies by the Office of the Public Welfare Commissioner on the Different Brands of Tiki-Tiki Extract.**—*Jl. Philippine Islands Med. Assoc.* 1932. June. Vol. 12. No. 6. pp. 273–281.

Tikitiki extract (extract of rice bran) has been very successful in the treatment of infantile beriberi in the Philippines. It is not surprising, therefore, that many brands of this product have appeared on the market. The present paper deals with experiments undertaken to show the efficacy, or otherwise, of the various preparations. The dosage used was as follows : to the mothers, besides a balanced diet, a tablespoonful of the extract was given after meals, while to the babies in mild cases 3–4 teaspoonsful were administered daily and in serious cases 5–7 teaspoonsful daily. On account of the laxative effect of tikitiki the above doses had sometimes to be modified in infants.

The results showed that the different brands of tikitiki extract have varying effects and it is therefore suggested that the preparation should be standardized to contain at least a given amount of vitamin B. It was also found that the extract is effective in the adult form of the disease and, therefore, should be given to women during pregnancy and lactation both for therapeutic and prophylactic reasons.

A. D. B.

VAN VEEN (A. G.). Over het B_1-vitamine-gehalte van geslepen rijst en van zilvervliesrijst. [**The Vitamin B_1 Content of Silverskin Rice and Polished Rice.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1932. Aug. 16. Vol. 72. No. 17. pp. 1146–1150. German summary. [Summary appears also in *Bulletin of Hygiene.*]

Machine milled rice frequently contains considerable anti-beriberi vitamin ; usually more than 0·5 mgm. per 500 gm. This residual vitamin can, of course, easily be removed by washing, whereas with unpolished rice this is not so. Washing milled rice appears to remove as much, if not more, vitamin B_1 as the original milling. The vitamin B_1 content of silverskin rice is at least as great as, if not greater than, that of Katjang-idjoe (*Phaseolus radiatus*), amounting to 1·5 mgm. per 500 gm. It was not found that red silverskin rice is particularly rich in vitamin, as is sometimes stated. Various sorts of rice meal, such as Katjang-idjoe meal, are not necessarily rich in vitamin B_1, though they are often used for their supposed richness in vitamin. It is desirable that many specimens of silverskin rice and polished rice from different sources be tested for their vitamin B_1 content. *H. N. H. Green.*

COHEN (A. J.) & AZIR. Bijdrage tot de kennis van de werking van vitamine-B (Jansen and Donath) bij beri-beri. [**Vitamin B (Jansen and Donath) in Beriberi.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1932. June 7. Vol. 72. No. 12. pp. 738–761. With 8 figs. on 4 plates.

The authors treated 18 beriberi patients with pure vitamin B, isolated by JANSEN & DONATH, partly by the way of intramuscular injections, partly in tabloid form. In uncomplicated cases the action of the injections was sometimes very striking; especially in cases of the acute cardiac type of beriberi (Shoshin) the preparation had a life-saving influence. Complications (hookworm disease, syphilis, etc.) interfered with the results. Administered in tabloids the purified vitamin may have a favourable influence on heart, blood pressure and diuresis. Probably the vitamin itself raises blood pressure in beriberi, possibly owing to its vasoconstrictory action. Sometimes actual hypertension may arise in this way, as well as by overfeeding with "kachang idjau." The importance of blood pressure control during treatment of beriberi cases is emphasized. *W. J. Bais.*

COWGILL (George R.). **Vitamin B_1 in Relation to the Clinic.**—*Jl. Amer. Med. Assoc.* 1932. June 25. Vol. 98. No. 26. pp. 2282-2288. [49 refs.]

This article is one of a series devoted to the application of vitamin study to clinical medicine. The subject of vitamin B_1 deficiency can best be considered under two headings: (i) where the deficiency is extreme, *i.e.*, beriberi, and (2) where the deficiency is only slight or moderate.

(1) An account of beriberi, including etiology, diagnosis and pathology is given. The disease is comparatively rare in the United States. Having regard to the separation of the original vitamin B into two fractions B_1 and B_2, it is interesting to note that cases have been recorded in which beriberi and pellagra exist together. Rice is deficient in both B_1 and B_2 vitamins but in the East fish forms a usual part of the diet and this being fairly rich in P-P factor accounts for the occurrence of beriberi and not pellagra. On the other hand corn meal, the staple food of pellagrins in the Southern States, is low in B_2 factor but when eaten in large amounts supplies an adequate quantity of B_1.

The relationship between beriberi on the one hand and fevers and gastro-intestinal disturbances, including jaundice and achlorhydria, on the other, is discussed. In general it may be said that individuals subsisting on diets in which the vitamin B content is too small or barely sufficient can be brought into a state of extreme deficiency when subjected to prolonged fever or heightened metabolism.

There are many conditions besides beriberi in which injury to the nervous system is a feature of extreme vitamin B deficiency; for example the spinal cord lesions in pernicious anaemia and the changes in the brain in pellagra. With regard to the clinical application of such studies it is stated that "in the face of the uncertainty as to what part is played by this vitamin in the nutrition of the nervous system, it seems justifiable to advocate administration of the vitamin in such cases, especially when this therapeutic measure is so easy to carry out and cannot do any harm."

(2) In the group in which vitamin B deficiency is slight or only moderate two main symptoms are discussed.

Anorexia.—It has been noted that in dogs fed upon a diet perfectly balanced except for vitamin B loss of appetite soon occurs and can be regained immediately by correcting this deficiency. The clinical application of this is obvious when due allowance is made for the fact that anorexia is usually only a symptom. Thus in marasmic infants, in cases of mental defect, during convalescence, etc., there is evidence to show that the administration of vitamin B has done much good. Another interesting observation is that when dogs fed on a vitamin B-deficient diet are given the missing factor they immediately consume large amounts of water and void much urine. This may have some relation to the oedema of beriberi and to the anhydraemia in certain marasmic infants. It is obvious that all the conditions already mentioned as favouring the development of beriberi (fever, heightened metabolism, etc.) also operate in bringing about a moderate shortage of vitamin B and, therefore, are of special interest to clinicians.

Restriction of growth.—While inadequate amounts of calcium and vitamin A may play an important part in limiting growth the studies of MORGAN and BARRY show that shortage of vitamin B can also be responsible in this respect in the case of American school children. The economic conditions associated with the present crisis are, as regards diet, more harmful to children in view of their lower tissue storage of vitamin reserve and their relatively greater need of this factor.

Finally the sources of vitamin B for clinical use are discussed. Yeast and wheat germ are two excellent sources of the vitamin. Larger amounts are contained in liver, kidney and brain than in muscle. Whole grains in contrast with milled varieties can supply appreciable amounts of this factor, while tomatoes, raw cabbage, fresh spinach and legumes are richer than orange and lemon juices, onions, lettuce or cauliflower. In the egg the vitamin is located in the yolk. Milk contains a good supply of B_2 factor but not B_1, therefore it is well to supplement the infants' milk diet. The importance of demanding proof that special concentrates of vitamin B on the market do actually contain this factor is stressed. *A. D. B.*

WENCKEBACH (K. F.). Der Mechanismus des plötzlichen Herztodes bei der Beriberi. [**Mechanism of Sudden Heart Failure in Beriberi.**] —*Klin. Wòch.* 1932. Sept. 24. Vol. 11. No. 39. pp. 1641–1647. With 5 figs. [14 refs.]

Prof. Wenckebach, of Vienna, under the auspices of the Queen Wilhelmina Jubilee Fund, was invited to visit the Dutch East Indies to study beriberi on the spot. The following constitutes a preliminary report of his researches concerning the mechanism of sudden, fatal heart failure in the disease.

"Shôshin," or sudden cardiac failure, occurs chiefly in young beriberi subjects who are apparently well and able to walk about. It is characterized by the most acute distress with severe pain in the chest and upper abdomen in the region of the liver. Death is very apt to occur. In order to obtain a clear *post mortem* cardiac picture the body was injected with formalin immediately after death. In nine cases so examined the findings were exactly similar except for variations in the size of the left ventricle. There was enormous enlargement of the right heart with great engorgement of the large veins and

liver, which latter was of globular shape. In order to prove that the injection itself played no part in these appearances, a heart in one of the cases was removed very soon after death and, though no formalin had been used, the organ had the appearance of having been forcibly distended and the wall of the right auricle was so thin that the blood could be seen through it. In addition, the right ventricle formed practically the whole of the heart when viewed anteriorly and the right conus arteriosus was markedly curved forwards. This last finding is very important as it is a never-failing component of the right-sided cardiac dilatation and is pathognomonic of the condition.

At Batavia the clinical side of the picture was studied. Twelve cases were analysed in which cardiovascular symptoms were practically the only sign of beriberi, there being no obvious oedema and no definite neuritis. The following are the chief findings: (1) The heart is enlarged, both clinically and radiologically. Even in slight cases the degree of enlargement is surprising, especially in the small-hearted Malay. (2) Various cardiac murmurs are heard, mostly systolic or presystolic in time, but in severe cases also diastolic. (3) Visible and palpable pulsation is present over the praecordium, particularly in the intercostal spaces on the left side. A strong apex beat may be felt but frequently it is absent. (4) Corrigan's collapsing pulse and a murmur heard over the large arteries are noted. (5) There is engorgement of the veins in the neck and arm while the liver is invariably swollen, painful and, in severe cases, pulsating. (6) Dyspnoea, with praecordial and epigastric pain, is the rule. (7) The calves are thickened and tender but there is no pretibial oedema.

Ordinary cardiac remedies are useless in "shôshin." Adrenalin makes the patient worse; indeed the effect of this drug on beriberi patients is so pronounced that in doubtful cases it may clear up the diagnosis. The hypodermic injection of 1 cc. of a 1 in 1,000 solution increases the cardiac rate and palpitation; the vascular murmurs become more pronounced reaching even "pistol shot" intensity; the diastolic pressure sinks almost to zero; the veins of the neck and arm swell visibly; the liver becomes larger and harder; the heart increases in size and the right side presents so that pulsation is seen to the left of the sternum. It is also recorded that the venous pressure (estimated with a needle in one of the large veins of the arm, according to the method of Tabora and Moritz), which is always high in beriberi patients, after adrenalin injection quickly rises still higher, from 6–16 cm. of water to 12–24 cm. All these findings are absolutely identical with those present in spontaneous "shôshin."

Very different is the effect of pitressin (P. D. & Co.). In severe cases almost immediately after injection the diastolic arterial pressure rises from about zero to 75 or even 90 mm.; the venous pressure suddenly falls; palpitation, dyspnoea and the feeling of tension in the upper abdomen, decrease; the area of cardiac dullness diminishes; the praecordial pulsation disappears and the lung margins once more cover most of the heart. In short, except for the heart remaining large, the patient has lost all his symptoms and this happy relief lasts from 25 minutes to 1¾ hours.

Two factors, it is claimed, are together responsible for the cardiac symptoms in beriberi: (1) a degeneration of the myocardium leading to a loss of muscular tone which normally prevents distension of the organ. In this way the heart, particularly on the right side, never

completely empties itself during systole. (2) Dilatation of the finer ramifications of the peripheral arterial system leading to an increased supply of blood which swamps the large veins, liver and right side of the heart. *A. D. B.*

WENCKEBACH (K. F.). Het raadsel van het stervende beri-beri-hart. [**The Riddle of the Failing Beriberi Heart.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1932. July 5. Vol. 72. No. 14. pp. 915–925. With 1 plate.

Prof. Wenckebach discusses the results of his study-tour through the East Indian Archipelago and comments in turn upon :

1. The beriberi heart after death, which shows an enormous dilatation in fresh cases, especially of the right half. The same condition exists in the venous system. This enormous afflux of blood is most surprising in view of the undoubtedly existing weakness of the heart.

2. The symptoms of the heart and vessels in recent acute cases. Such are more frequent than is commonly known. Dilatation of the heart, murmurs, strong pulsations, a hammering pulse and bruits over the larger arteries, overfilling of the venous system, with painful swelling of the liver, shortness of breath, palpitations and swelling of the muscles of the calves—symptoms which are harmfully influenced by the slightest bodily exertion of the patient—constitute a most confusing condition for medical interpretation.

3. AALSMEER's adrenalin test (see this *Bulletin*, Vol. 29, p. 614) is able to bring about a recrudescence with all the acute symptoms in cases on the way to recovery. The lowering of the blood pressure in the arterial system with simultaneous increase of the venous pressure is caused by a " leakage " of the arterial reservoir into the venous system, *i.e.*, by an important dilatation of the peripheral circulation (small arteries and pre-capillary vessels).

4. The pitressin test, *i.e.*, the injection (with caution !) of the vasomotor substance from the posterior lobe of the hypophysis (Parke Davis) has exactly the contrary effect and is able to cause a sudden disappearance of the symptoms for some time.

5. The degeneration of the heart and skeletal muscles is characterized by a retention of water *within* the muscle cells, in contrast with oedema of the muscle which is an accumulation of water between the muscle fibres. This condition is a very typical disturbance of the metabolism of the muscular system in beriberi. It is not justifiable, however, to ascribe the paralysis of the vessels to the same cause, in view of their prompt reaction to pitressine and the different anatomical structure of their muscular wall.

6. The beriberi of nurslings is to be considered as a proof of the existence of much latent beriberi among the natives. Its diagnosis is difficult and its symptomatology still very uncertain. Yet undoubted reactions to the administration of vitamins have been noticed.

7. In beriberi cases of some duration the overstretching of the muscle fibres of the heart is liable to cause lasting damage to this organ. Medical care is urgent in such cases. Besides vitamin administration, the use of pitressin deserves attention and further study. Yet in view

of its vasoconstrictor action, exerted upon the coronary arteries as well as upon the other parts of the arterial system, it should be used with much caution and only in cases of general weakness of the heart.

W. J. Bais.

AALSMEER (W. C.) & RICHTER (C. S.). Over den invloed van Lugoloplossing op het adrenaline effekt bij Basedow en beri-beri.—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1932. Aug. 30. Vol. 72. No. 18. pp. 1214–1218.

HASCHIMOTO (T.), AIZUMI (H.), DENDO (K.) & FURUNO (M.). Beiträge zur Studien ueber die Colibazillen im Kot der Beriberikranken und dem der nicht an Beriberi leidenden Menschen.—*Jl. Oriental Med.* 1932. Aug. Vol. 17. No. 2. [In Japanese. German summary p. 14.]

PLAGUE.

FOURIE (L.). **Report on Plague in Ovamboland, South West Africa.**—*Union of South Africa. Ann. Rep. Dept. Public Health Year ended 30th June, 1932.* Annexure A. pp. 58–80.

The report is one which tells of an expedition by train of 500 miles to examine into an outbreak of plague in the tribal country of Ovamboland. In its beginnings the epidemic had been so mild as to be mistaken for something of the nature of climatic bubo. Lack of information is only to be expected when the epidemiology of a disease is being investigated among a primitive people, but some useful data have been accumulated. In much of the country affected the abundance and luxuriance of grass vegetation or the suitability of the soil for burrowing afforded favourable conditions for the indigenous rodents. The nature of the food supply and the primitive mode of living of the people are selected for notice as having "an important bearing on the spread of plague from rodent to man in Ovamboland." The staple food is a millet. Small rodents such as gerbilles are caught by digging up their burrows and these are eaten by both children and adults. Meteorological conditions were favourable to the continuance of plague during the year. Mean temperatures ranged from 60° to 80°F. and the saturation deficiency exceeded 0·3 of an inch only in the last three months of the year. An enumeration of the small mammals associated with the spread of plague in the Union together with their distribution is given. The multimammate mouse (Mastomys) "is virtually the domestic rat of Ovamboland." It seems too to be the most important intermediary between wild rodents such as the gerbilles and man. Of fleas which have been shown capable of transmitting plague from rodent to rodent the following were identified: *Ctenocephalus canis, Dinopsylla brasiliensis, Xenopsylla eridos* and *X. brasiliensis*. It is interesting to learn that the local view of the origin of the present outbreak is that infection "was introduced through mealie meal imported from the Union during the famine period of 1929–30," but this view is dismissed as untenable. The conclusion come to was that the available evidence points to the kraal rather than the outside veld being the most important source of infection and that this has been consequent upon the mortality among kraal rodents. *W. F. Harvey.*

ESKEY (C. R.). **Epidemiological Study of Plague in Peru, with Observations on the Antiplague Campaign and Laboratory Work.**—*Public Health Rep.* 1932. Nov. 18. Vol. 47. No. 47. pp. 2191–2207. With 12 figs. on 2 plates & 1 map.

Plague was first introduced into the port of Callao in 1903 and spread rapidly north and south. It reached its height six years after its introduction and has for the most part been restricted to the sea coast provinces and to adjacent mountain provinces north of 12° south latitude. A good plate of all the different species of flea occurring in Peru is given, but *X. cheopis* is probably the only transmitting agent which need be considered. Of rats which were concerned in plague transmission, *R. alexandrinus* and *R. rattus* were the predominating species, caught in those localities where the buildings were most infested. It was in those towns in which this infestation of the buildings was greatest that the incidence of plague was also

greatest and this "regardless of the climatic location of the towns within or outside the zone most favourable to the existence of the chief transmitting agent *X. cheopis*." A relative rat-proof construction of buildings is obviously a means of attaining to low incidence or even complete absence of human plague in Peru. Active antiplague measures began at the end of 1930 or beginning of 1931 and the results obtained in the first six months have been very good. The use of poison for the destruction of rats appears to have yielded very good results. Arsenic is the poison used and experiments have shown that a coarse cornmeal was the best material for making up the baits. Other details are given of the organization of this campaign. Chronic plague infection has never been found and mass inoculation of a suspension from small pieces of spleen and liver of all autopsied rats has been made daily into a guineapig. *W. F. H.*

MACCHIAVELLO VARAS (Atilio). Ensayo sobre la peste en Chile. [**Plague in Chile.**]—*Bol. Oficina Sanitaria Panamericana.* 1932. Sept. Vol. 11. No. 9. pp. 909–915.

This is an interesting general account of plague in Chile, treating of its history, the species and relative numbers of the rats and their fleas, and epidemiological considerations. Infection is said to have first entered Chile via Iquique and Valparaiso in 1903, later involving all the ports north of Coquimbo and appearing time and again transiently in the capital. It died out in Iquique in 1922 having caused 1,500 cases and 600 deaths. It reached Antofagasta in 1904, the most recent outbreak occurring in 1930; there have been 1,500 cases and more than 700 deaths. In Valparaiso plague has not been continuous and the total number attacked is barely 100. In Santiago it caused 23 cases in 1907 and in 1931 it was of the pneumonic type; there has been no serious epidemic in the capital.

The total number of cases in Chile is about 5,200, with some 40 per cent. (2,150) fatal. The maximum occurred in 1907 with 861 cases and 358 deaths. In the first five years there were over 2,250 cases, in the next five 2,140, in the third barely 400 and since 1918 not more than 300. Except for the last (pneumonic) outbreak in Santiago, the form has been bubonic with a few septicaemic.

As regards the species of rats, in Antofagasta in 1929 of nearly 5,000 examined the percentages were 21·6 *R. norvegicus*, 12 *R. alexandrinus*, 27 *R. rattus*, 39·4 *Mus musculus*. The first predominated in the commercial centres and on the quays and wharves, *R. rattus* in the city generally. In 1931 among nearly 10,000 examined *norvegicus* fell to below 17 per cent. and a marked diminution of them was noticed on the quays. In 1930 there were 86 found infected; more than half were *R. norvegicus* and one-fourth *R. rattus*.

The average number of fleas per rat was 20; on *R. norvegicus* 13·3, on *R. rattus* 35·1, on *R. alexandrinus* 31, on *Mus musculus* 12·5; *X. cheopis* was the commonest, 11, *L. musculi* next 2·3.

The author attaches great importance to climate in the epidemiology of plague, "relative humidity and the maximum and minimum temperatures governing the appearance or latency of plague in the northern ports." Whenever the minimum exceeds 15° and the maximum 25° with a relative humidity of 70 per cent. or thereabouts plague reappears. This, in his opinion, helps to explain its disappearance in the last 10 years during which the Chilian climate has

altered in the north, being generally more temperate and colder and "thus unfavourable to development of the activities of *X. cheopis*." But many problems cannot be so explained: At Valparaiso the bionomics of *C. fasciatus* have to be taken into account; at Santiago there is much seasonal variation. The excessive heat of the summer is inimical to plague, whereas the winter favours pneumonic plague "but doubtless there are complications which call for detailed study."

H. H. S.

MATHIS (C.) & ADVIER (M.). Considérations épidémiologiques sur la peste au Sénégal (à propos du mémoire de G. Lefrou présenté à la séance du 8 juin 1932). [**Epidemiology of Plague in Senegal.**] —*Bull. Soc. Path. Exot.* 1932. Nov. 9. Vol. 25. No. 9. pp. 941–944.

This article is mainly concerned with the refutation of the idea that human plague in Senegal was not a consequence of plague in rats, but was one of transmission from case to case directly by human fleas. The evidence for the commonly accepted view is taken up point by point. *W. F. H.*

DELANOË (P.). L'importance de la puce de l'homme. *Pulex irritans* L., dans les épidémies de peste au Maroc. [**The Importance of the Human Flea.** *Pulex irritans*, **as a Vector of Plague in Morocco.**] —*Bull. Soc. Path. Exot.* 1932. Nov. 9. Vol. 25. No. 9. pp. 958–960.

The author has long insisted on the importance of the human flea in propagating plague by transmission from case to case. In Morocco the numbers of *Pulex irritans* infesting the houses is almost incredible. This fact together with the known shortness of time that this flea remains infective are, according to the author, reasons why plague in certain parts of Morocco has been severe and yet has then disappeared completely for a period of years. *W. F. H.*

NOVIKOVA (E.) & LALAZAROV (G.). **The Rôle of Bedbugs in the Epidemiology of Plague. I. The Duration of Viability of Plague Virus in the Body of the Infected Bedbug.**—*Rev. Microbiol., Epidémiol. et Parasit.* 1931. Vol. 10. No. 4. pp. 315–322. With 1 fig. [24 refs.] [In Russian. English summary pp. 323–324.]

Cimex lectularius, the bedbug used, was kept without food and then fed on infected mice or rats as soon as a bacteriaemia had manifested itself. Plague bacilli were successfully isolated from the faeces of the bugs in 37 per cent. of cases and the number of bacilli was at its greatest in the faeces from the 5th to the 12th day after infection. The bodies of dead bugs were emulsified in salt solution and agar plates sown with this emulsion. An abundant growth of plague bacilli was obtained in most cases. It was found that the plague virus "may remain virulent in the body of the bedbug for as long as 147 days" after feeding. In these experiments three of the infected bugs lived 186, 222 and 250 days respectively, but inoculation of animals with, and bacteriological examination of, the emulsions of these bugs gave negative results. Transmission of plague by the bite of an infected bug was successful in one case. *W. F. H.*

TUMANSKY (V.) & POLIAK (I.). **On the Preserving of Plague Virus in the Organism of Fleas in Suslik Nests at Non-Epizootic Period.**—*Rev. Microbiol., Epidémiol. et Parasit.* 1931. Vol. 10. No. 4. pp. 325–326. [In Russian. English summary p. 326.]

A severe plague epizootic had occurred and had ceased by June. In the region of the epizootic 31 nests of susliks were dug out, 13 in November, 7 in December, 5 in January and 6 in February and yielded a total of 1,797 fleas for examination. The bacteriological examination of an emulsion of the alimentary canal showed 5 of the November fleas (2 *Neopsylla setosa* and 3 *Ctenophthalmus pollex*) to be plague infected, although their proventricles were free of the characteristic plugs. *W. F. H.*

KOPSTEIN (Felix). De rattendichtheid als factor in de epidemiologie der builenpest. [**Rat Density as a Factor in the Epidemiology of Bubonic Plague.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1932. July 19. Vol. 72. No. 15. pp. 960–968.

7,852 native dwellings in W. Java were examined for the number of rats they harboured; approximately 1,100 were examined 2–5 times for control of the results. The local rat density was found to be fairly constant; no great seasonal differences throughout the year were found, apart from epizoötics. Therefore the rat density may be considered as a useful factor in epidemiological research. Care must be taken to use different types of traps if catches follow each other in quick succession. The density of *R. rattus* is lower in places where plague has been prevalent. Yet such low density is no proof of epidemics in the past. *W. J. Bais.*

KOPSTEIN (Felix). Die geographische Verbreitung von *Xenopsylla astia* in Java und ihre Bedeutung für die Epidemiologie der Beulenpest. [**The Geographical Distribution of *Xenopsylla astia* in Java and its Significance in the Epidemiology of Plague.**]—*Ztschr. f. Hyg. u. Infektionskr.* 1932. Aug. 22. Vol. 114. No. 2. pp. 289–301. [41 refs.]

In 20 years of its history in Java plague has never become established on the southern coast of the island, in spite of all the rat-fleas there being *Xenopsylla cheopis*; on the northern coast it has occurred in some port towns but not in others. The purport of this long account of the geographical distribution of *Xenopsylla astia* in Java is to throw some light on this relative immunity of the coastal zone of the island from plague; it takes the British reader among very unfamiliar geography and place names. So far as is known *X. astia* occurs only on the coastal zone. On the northern coast, where seaports in communication with Asia are numerous, it is found in many of them, but not in Batavia and Passoeroean where the only rat-flea known is *X. cheopis*. On the southern coast, where there are only two seaports and one of them of small importance, it has so far not been found, at any rate in these ports. The house-fauna of the northern coast includes 3 rats—*Rattus diardi*, *R. concolor*, and *R. norvegicus* and the house-shrew *Pachyura murina*; in that of the southern coast *R. concolor* and *R. norvegicus* are wanting; but the absence of these two species has no significance since *R. concolor* is accompanied by *X. astia* in some places on the northern coast and *R. norvegicus* by *X. astia* in many of the

northern ports. On the northern coast, again, besides Batavia and Passoeroean where *astia* is unknown, there are two other ports where the percentages of *astia* are only 8·8 and 14·6 against corresponding percentages of 91·2 and 85·4 for *cheopis*, all these four places having suffered from epidemics of plague. Furthermore, in six ports where plague has *not* occurred, *X. cheopis* is the only species known in two of them, and in the other four has percentages of 96·0, 87·4, 75·2, and 39·3 against correlated *astia* percentages of 4·0, 12·6, 24·8, and 60·7 (Banjoewangi). These facts of geographical distribution do not suggest that *X. astia* has any influence on the epidemiology of plague in Java. With regard to the theory of import of *X. astia* by sea, its absence from the large seaport Batavia and also from Passoeroean requires explanation. Attention is drawn to the fact that although *X. astia* has been found in nature only in the hot and moister climate of the coast of Java it has lived on a house-rat in a laboratory in Bandoeng at a height of 700 metres for a year; and this supports the inference that it may come to light in the inland of Java sooner or later. The author indeed appears to think that climate and season have some influence on the sporadic distribution of this species in Java.

Of fleas taken from 974 house-rats and 275 house-shrews in the coast zone of Java 2,279 were *X. cheopis* and 590 were *X. astia* (also 1 *Ct. felis*). *A. Alcock.*

i. KOPSTEIN (Felix). De biologie van de Huisspitsmuis Pachyura Murina (L.) en hare beteekenis voor de epidemiologie der builenpest op Java. [**The Biology of the House Shrew** (*Pachyura murina* **L.**) **and its Significance for the Epidemiology of Bubonic Plague in Java.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1932. Sept. 27. Vol. 72. No. 20. pp. 1337–1349.

ii. SCHUURMAN (C. J.). Eenige opmerkingen naar aanleiding van twee artikelen van Kopstein op het gebied der pest-epidemiologie. [**Comment upon Two Articles by Kopstein, Concerning the Epidemiology of Plague.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1932. Sept. 27. Vol. 72. No. 20. pp. 1350–1358.

i. The author relates the results of a survey of over 10,000 houses in Java in places where *P. murina* was found besides *M. rattus*. The shrew was found to nestle exclusively in native villages outside as well as inside the native dwellings. It is more often found on the ground level than in higher parts of the house, never in the roof. It very rarely leaves the villages for the open field.

About 46 per cent. of them are flea carriers, the most common flea being *X. cheopis* (average flea index 1·7). These figures are lower than those of *M. rattus*. As a transmitter of fleas among rats the shrew may play a part, but it has relatively little contact with man. In the spread of plague from village to village it has apparently no practical significance.

ii. Schuurman's article is a polemic one which cannot be summarized in detail. He does not agree with Kopstein as regards the relative numbers of shrews and rats in the villages nor as regards the changes in density of shrew population (which he would take as indicating active migration of the animals). He also found a much higher flea index. *W. J. Bais.*

FONQUERNIE (J.). Essais de traitement de la peste par le bactériophage. [**Treatment of Plague by Bacteriophage.**]—*Bull. Soc. Path. Exot.* 1932. July 6. Vol. 25. No. 7. pp. 677–678.

The article gives details of five cases of plague which were treated ineffectually with bacteriophage. This administration was intrapulmonary, subcutaneous, intravenous, intramuscular and oral.

W. F. H.

RAO (B. R. Ranganatha). **Three Cases of Plague treated with "Bayer 205."**—*Indian Med. Gaz.* 1932. Nov. Vol. 67. No. 11. p. 626.

None of the three cases had been inoculated against plague. The treatment consisted of an intravenous injection of 0·9 gm. "Bayer 205" in 10 cc. distilled water. The first two cases recovered rapidly and the third also recovered with some delay. *W. F. H.*

LEGENDRE (F.). Sur un cas de diagnostic de peste par examen du sang. [**Plague diagnosed by Blood Examination.**]—*Bull. Soc. Path. Exot.* 1932. Nov. 9. Vol. 25. No. 9. p. 1012.

A patient was having his blood examined for malaria parasites shortly before his death. The smears, however, showed the blood to be swarming with plague bacilli and the case was obviously one of agonal septicaemia. The author calls attention to the dangers which may result to the investigator and others from such cases. *W. F. H.*

DE SMIDT (F. P. G.). **Nairobi Plague Prophylactic: Further Notes on Preparation and Potency.**—*East African Med. Jl.* formerly *Kenya & East African Med. Jl.* 1932. Nov. Vol. 9. No. 8. pp. 227–236.

Many useful laboratory details are given of the preparation and immunizing value of variously treated plague vaccine. The incubation of cultures continuously at 30°C. for six weeks yields a vaccine superior to that with incubation partly at 30°C. and partly at the variable atmospheric temperature of Nairobi for a total of 12 weeks. Immunizing potency of a vaccine is diminished by heating at 55°C. for 1 hour, and almost destroyed by heating at 100°C. for the same period. A comparison of the immunities produced by small and large doses of vaccine suggested that this was not high for the latter, considering the extra toxicity of the large dose. Intraperitoneal inoculations could be depended on to be invariably successful in affording rat spleens containing plague bacilli, which are used in inoculating vaccine cultures. This was not the case with subcutaneous injection.

W. F. H.

BUCHANAN (George S.). La préparation du vaccin antipesteux à l'Institut Lister. [**Preparation of Plague Vaccine at the Lister Institute.**]—*Bull. Office Internat. d'Hyg. Publique.* 1932. Oct. Vol. 24. No. 10. pp. 1626–1630. With 2 diagrams.

When it is grown at 37°C. instead of at 26°C. or even 30°C. the plague bacillus develops a gelatinous envelope and it would seem

that this gelatinous material is the most important antigen of immunization [see this *Bulletin*, Vol. 29, p. 676]. Quite possibly Haffkine's broth vaccine, as manufactured in Bombay, would be improved by cultivation at this temperature. In the Lister Institute the Bombay vaccine was found to be certainly superior to a vaccine prepared from cultures on agar. Another vaccine altogether, which is regarded as of high prophylactic power and non-toxic, is the lysate of plague bacilli produced by a suitable bacteriophage. *W. F. H.*

i. GRAHAM. Enquête sur les résultats de la vaccination antipesteuse. La vaccination antipesteuse dans un district du Pendjab. [**Enquiry into the Results of Plague Vaccination in a District of the Punjab.**]—*Bull. Office Internat. d'Hyg. Publique.* 1932. Oct. Vol. 24. No. 10. pp. 1606–1609.

ii. BOYÉ. Les résultats des vaccinations antipesteuses dans les colonies françaises. [**Results in the French Colonies.**]—*Ibid.* pp. 1610–1622.

iii. STOCK (P. G.). Résultats de la vaccination antipesteuse dans l'Union de l'Afrique du Sud. [**Results in S. Africa.**]—*Ibid.* pp. 1623–1625.

In these communications further replies to a questionary [see this *Bulletin* Vol. 29, p. 674] are given. Some of these may be picked out.

i. Among 20 villages in the Punjab with populations varying from 170 to 3,100 there was not a single case of plague among vaccinated persons in fourteen, whilst the morbidity among non-vaccinated ranged from 4·27 per cent. up to as much as 56 per cent. Most of the cases of plague in the vaccinated had no fever. The author concludes that plague vaccination is of great value.

ii. Among 237 patients in hospital and treated identically there were 128 vaccinated and 109 non-vaccinated with mortalities of 37·5 and 52·2 per cent. respectively.

In the report of the Director-General of Health in Indo-China a number of instances are cited, where vaccination appeared to be efficacious. Stress is laid upon the use of the word "appeared" because interpretations might differ regarding the facts. An example is given and the qualifying remark is made: "If the effect of vaccination was truly a positive one then the duration of the immunity must have been short, seeing that less than three months after their inoculation the inhabitants had again become susceptible." Again the author writes: "It is very difficult to draw any conclusions from the reports of Senegal: certain facts tend to prove that the vaccine has only a very doubtful efficacy."

iii. Prophylactic vaccine has been used in S. Africa on a rather large scale. The results have not been conclusive. *W. F. H.*

TAYLOR. Enquête sur l'efficacité de la vaccination antipesteuse. Deuxième réponse de l'Institut Haffkine de Bombay. [**Anti-Plague Vaccination Inquiry. Second Report from Bombay.**]—*Bull. Office Internat. d'Hyg. Publique.* 1932. Nov. Vol. 24. No. 11. pp. 1813–1860.

The vaccine used is a broth culture of 4 weeks' incubation at 26·6°C., sown with a virulent strain of *Past. pestis* and killed by heat followed

by the addition of phenol. The ordinary statistics of plague, inasmuch as they do not furnish information of the comparative degree of risk to which the vaccinated and the non-vaccinated population has been subjected are almost valueless. The statistics, on the other hand, of special vaccination campaigns have, according to the author, a true statistical value. Careful details are given of these at very considerable length. They are summarized in Table XVIII (slightly

Recapitulation of statistics of epidemics for which reliable and comparable data exist.

Epidemics	Population		Vaccinated		Non-vaccinated	
	Vaccinated	Non-vaccinated	Cases	Deaths	Cases	Deaths
Reformatory at Byculla (1897)	147	172	2	—	12	6
Lanowli (1897)	323	377	14	7	78	57
Umerkhadi prison (1898)	147	127	3	—	10	6
Undhera (1898)	71	64	8	3	27	26
Hubli (1898) ...	24,631	17,786	lacking	338	lacking	2,348
S.M.R. Hubli (1898)	1,260	760	11	2	35	21
Belgaum (1899)	4,842	4,558	78	40	506	346
Jewish Community at Aden (1900)	1,190	982	23	8	83	65
Nawashahr (1900)	2,648	2,141	9	5	41	32
Kahma (1900) ...	863	889	—	—	10	5
Khatkar Kalan (1900)	1,040	338	6	2	6	5
Salem (1910) ...	27,489	27,181	434	226	1,693	1,495
Coimbatore (1913–14) ...	26,559	22,604	150	56	707	492
Bagdad (1919) ...	56,555	108,445	65	36	806	638
Totals	147,765	186,424	—	723	—	5,542
Totals (Hubli excluded) ...	121,134	168,638	803	385	4,014	3,194

modified) and the conclusion is drawn that vaccination diminishes the chances of contracting plague 4 times and the chances of dying by 8 times. *W. F. H.*

PANAYOTATOU (Angélique). Sur une épidémie de peste à l'île de Poros (Grèce) en 1837 (d'après les notes du calendrier d'un médecin de l'époque). [**An Epidemic of Plague in Poros in 1837.**]—*Rev. Prat. Malad. des Pays Chauds.* 1932. Feb. 11th Year. Vol. 12. No. 2. pp. 60–62.

Even at this early time the method of disinfecting persons suspected of plague and their effects was, very reasonably, by means of chlorine water. The fear which the epidemic inspired is manifest in the action of the members of committee deputed to conduct the inspection who, armed with two pistols, examined the axillae and the buboes with the pointed end of a cane. *W. F. H.*

JETTMAR (H. M.). Pestprobleme in der Mandschurei. [**Plague in Manchuria.**]—Reprinted from *Wien. Med. Woch.* 1932. No. 19. 10 pp.

This is an epidemiological study of plague, which covers the ground of the animals infected in nature, the carry-over of plague in the winter months and the difficulties of the plague campaign. *W. F. H.*

ANNALES DE MÉDECINE ET DE PHARMACIE COLONIALES. 1932. Jan.–Feb.–Mar. Vol. 30. No. 1. pp. 101–107.—La peste au Sénégal en 1930. Extrait du rapport annuel de M. le lieutenant-colonel PEYRE, chef du service de santé p.i.

DE LA TORRE (Francisco). Proyecto de profilaxis de la peste bubónica para la provincia de Córdoba.—*Semana Méd.* 1932. Sept. 1. Vol. 39. No. 35 (2016). pp. 610–614. With 1 map.

JOSEPH (Gaston). Mesures administratives prises au Sénégal et à Dakar contre la peste en 1931.—*Bull. Office Internat. d'Hyg. Publique.* 1932. Oct. Vol. 24. No. 10. pp. 1631–1633.

LAUZERAL (P.) & MILLISCHER (P.). A propos de la filiation de deux cas de peste, l'une à allure septicémique, l'autre à allure pneumonique.—*Bull. Soc. Path. Exot.* 1932. Nov. 9. Vol. 25. No. 9. pp. 935–941.

REYNAL (J.) & WASSILIEFF (A.). Prophylaxie de la peste à Tunis. La station municipale de surveillance murine : laboratoire du rat : son fonctionnement pendant une année (mai 1931–avril 1932).—*Arch. Inst. Pasteur de Tunis.* 1932. July. Vol. 21. No. 1. pp. 181–207. With 1 chart. [10 refs.]

CHOLERA.

JUDE (L. V. R.), MARTIN (L. H. D. H.) & MILLISCHER (P.). La défense des territoires du Levant placés sous mandat français, contre l'épidémie de choléra ayant sévi en Irak. (Juillet–Décembre 1931). [**Defensive Measures for French Mandated Territories against Cholera in Irak.**]—*Arch. Méd. et Pharm. Milit.* 1932. Dec. Vol. 97. No. 5. pp. 521–536. With 1 folding map.

The motor route by the desert from Baghdad to Damascus is now of the utmost importance in connexion with the spread of cholera. An epidemic of cholera broke out at Basra, which had a weekly incidence of 265, 294, 200, 142, 294, 354, 210 and 120 cases from 9th August to the 3rd October. It spread up the Tigris and Euphrates and down the Shatt-el-Arab. As a result of this generalization of the epidemic special precautions were taken in the French mandated territories. Investigation too was instituted into the subject of the healthy carrier and a surprising result was obtained. From the first several carriers were found, the majority coming from non-infected localities, presenting no symptom of illness and in possession of regular certificates of vaccination. Out of a total of 1,560 travellers 5·38 per cent. were declared carriers, but this percentage reached as high as 20 per cent. in one week. The carrier percentages had a degree of parallelism with the intensity of the epidemic. This high proportion led to the examination of all travellers without distinction and necessitated a great effort in organization. Most travellers arrived in the early morning; their stools were immediately cultured and 8 hours later all those with negative findings were immediately released from quarantine restriction. Suspicious cases and carriers were detained for 2 or 3 days and given cholera vaccine *per os* by Besredka's method. Their stools became rapidly free of vibrios. Success crowned the efforts made and the barrage was completely suspended when Iraq was declared free of infection. The method of examination was to make a culture of the stool in peptone water (pH 8·2) and incubate 8 to 10 hours. No pellicle has yet formed by that time, but fine strands of growth may be detected on the surface. Gram staining and examination for motility were then carried out and if all the tests were negative the traveller was released. If Gram-negative, motile vibrios were found, even in the absence of a surface growth pellicle, further testing was undertaken. Of the strains isolated some were sent to the quarantine laboratory at Alexandria and some to the Pasteur Institute in Paris where confirmation that they were cholera vibrios was obtained. [These findings raise many important questions, not only those of the identification of the cholera vibrio, agglutination tests and standard sera, but also whether these vibrios are pathogenic and if not, whether they may become so.]

W. F. Harvey.

BIFULCO (C.). Patogenesi del colera asiatico. Nota I. [**Pathogenesis of Cholera.**]—*Riforma Med.* 1932. Aug. 27. Vol. 48. No. 35. pp. 1323–1326, 1329.

Difficulty has always been experienced in producing anything like the true cholera syndrome in animals. The author has succeeded in overcoming this difficulty by injecting a suspension of cholera vibrios into the superior mesenteric vein of rabbits and thus approaching

the liver by the portal circulation. In this way there is little loss in concentration of the vibrio dose. The result is markedly different from that obtained when injections are made into the ear vein, into the heart or into the peritoneum ; in fact an attack of cholera is produced similar to that seen in man. The liver therefore is highly important in the pathogenesis of cholera. The vibrios are brought into association with the liver cells in a functional sense, which is not the case with introduction into the general circulation. Their activity is exalted and they are passed into the intestine by way of the bile to set up the characteristic cholera syndrome. *W. F. H.*

GOHAR (M. A.). **Some Observations on the Haemolysin and Toxin of Cholera and Related Organisms.**—*Zent. f. Bakt.* I. Abt. Orig. 1932. Oct. 25. Vol. 126. No. 1/2. pp. 61–68.

In the group of cholera and cholera-like vibrios, taken as a whole, the individual members or strains may be non-haemolytic or they may be more or less haemolytic. The cholera vibrio is a non-haemolytic, non-toxic organism, while the El Tor vibrios, which are closely related to the cholera vibrios biochemically and serologically, are both strongly haemolytic and productive of an exotoxin. This work is in the main a study of the conditions under which haemolysin is produced and of its relation to exotoxin.

It is known that true cholera vibrios, although non-haemolytic, produce a halo of clearing around colonies on a blood agar plate. The same sort of halo is produced by the haemolytic vibrios if grown anaerobically, that is to say, under unfavourable conditions. It is suggested from this that the true cholera vibrio is not absolutely non-haemolytic but that it produces a small amount of haemolysin. With the aid of concentration methods and freshly isolated strains this was found to be probable. The relationship of haemolysin and exotoxin is considered to be very close : in fact they are regarded as one and the same. Highly haemolytic vibrios, therefore, produce a powerful exotoxin and non-haemolytic vibrios no exotoxin. It seems likely that the phenomenon of haemolysis by vibrios is due in the first place to affinity of the lipoid membrane of the erythrocyte for haemolysin. Lipoids or lipoid-containing tissues, such as cholesterol, suprarenal tissue and cerebral tissue are capable of adsorbing considerable amounts of haemolysin, whereas kaolin and neutral fats are not. With adsorption by lipoids the toxin and haemolysin of cholera-like vibrios are rendered atoxic and non-haemolytic. The evidence, although not wholly conclusive, is then very suggestive of the identity of vibrio haemolysin and vibrio exotoxin. The objection that an old haemolytic vibrio may lose its toxicity and yet remain haemolytic is discussed. It still retains, however, the power to confer immunity against the toxin, which points rather to a " degradation in the quality of toxin than actual loss of the power of its production."

W. F. H.

GOHAR (M. A.). **A Serological Study of *V. cholerae* and Related Vibrios.** —*Brit. Jl. Experim. Path.* 1932. Aug. Vol. 13. No. 4. pp. 371–379. [Summary appears also in *Bulletin of Hygiene.*]

Of 45 strains examined 35 gave the typical biochemical reactions of cholera, and of these latter 23 were haemolytic and 12 non-haemolytic. More detailed investigation of the antigenic structure of the

test strains showed that true non-haemolytic cholera vibrios all possessed the same flagellar and somatic antigen. The cholera-like organisms may possess either flagellar or somatic antigen in common with the cholera vibrio and require an absorption test for their differentiation. None of the haemolytic vibrios of the series examined possessed antigen identical with the cholera vibrio. *W. F. H.*

ZIMMERMANN. Untersuchungen zur Cholera-El-Tor-Frage. [**The Cholera-El Tor Question.**]—*Zent. f. Bakt.* I. Abt. Orig. 1932. Vol. 127. No. 1/3. Beiheft pp. 146*–149*.

The author shows clearly how important it is to establish controls upon the production of haemolysis by vibrios. The composition of the culture medium is especially important. Under strict conditions of testing the great majority of the strains labelled cholera never showed haemolysis, while in the same way almost all the El Tor strains produced a strong haemolysin. *W. F. H.*

GOYLE (Amar Nath) & GUPTA (P. N. Sen). **Notes on Spontaneously Agglutinating Strains of *V. cholerae* both Natural and Artificially Produced.**—*Indian Jl. Med. Res.* 1932. July. Vol. 20. No. 1. pp. 35–41. With 3 figs.

The authors describe a form of *V. cholerae* obtained by the methods used to effect dissociation. This form, although it did not produce characteristic rough colonies on agar, was nevertheless spontaneously agglutinable. They suggest that roughness "may sometimes only be shown by serological investigation." *W. F. H.*

YU (H.) & CHEN (K. F.). **A Suggestive Skin Test for Susceptibility to Cholera.**—*Chinese Med. Jl.* formerly *Nat. Med. Jl. China.* 1932. Aug. Vol. 46. No. 8. pp. 799–805. [11 refs.] [Summary appears also in *Bulletin of Hygiene.*]

The toxic material used in test was obtained from specially selected cultures of the cholera vibrio whose virulence had been raised by animal passage. It was shown that the presence of glucose in the nutrient medium interfered with the production of toxic substance and a buffered broth without glucose, with an initial pH 8·4, was finally used. After 6 hours incubation the culture was centrifuged at high speed and the supernatant liquid filtered through a Berkefeld N candle. This filtrate was still lethal to guineapigs in a dose of 5 cc., after heating for one hour at 80°C. In the skin tests it was found that rabbits gave a negative or positive skin reaction with the toxic filtrate according as they had or had not been immunized previously with cholera vaccine. In human beings also a skin test carried out on unvaccinated and vaccinated persons, by injecting intradermally 0·1 cc. of toxic filtrate, gave positive and negative reactions respectively. Persons vaccinated two and even three years previously still gave negative skin reactions, from which it would seem that the intradermal cholera test may be a very delicate indicator of the duration of immunity. "Further study may prove the value of the skin test as a method of testing individual susceptibility to cholera." *W. F. H.*

HURI (Maurice). Etude d'un vibrion (*n. sp.*) isolé à Damas (Syrie), dans dix-neuf cas de diarrhée chez l'homme. [**A New Vibrio isolated at Damascus from Nineteen Cases of Diarrhoea.**]—*C. R. Soc. Biol.* 1932. Dec. 2. Vol. 111. No. 37. pp. 678–680.

In these cases the diarrhoea was abrupt in onset, accompanied by violent colic, and the stools were as many as 20 daily. It gradually subsided but remained for several weeks. Smears showed a regular feltwork of vibrios. These possessed usually single cilia and were not to be found in stream and well water. A very fine pellicle was formed in peptone water culture. The nitroso-indole reaction was feeble or absent. Other cultural characters were that it did not coagulate milk, did not change the colour of litmus milk, did not show any proteolytic character and did not liquefy gelatin. It was not haemolytic and did not agglutinate with cholera serum. In only one case was it possible to test the patient's own serum, which agglutinated his own vibrio at 1 in 350. This same serum agglutinated two of the other isolated strains at 1 in 100 and 1 in 150. *W. F. H.*

VEDDER (A.) & VAN DAM (W.). De beteekenis der pH voor de rijping en electiviteit van cholera-voedingsbodems. [**The Importance of the pH for the Ripening and Selectivity of Cholera Nutrient Media.**]—*Nederl. Tijdschr. v. Hyg. Microbiol. en Serol.* 1932. Vol. 7. No. 2. pp. 147–164.

—— & ——. Studien ueber Elektivnährböden für Choleravibrionen. I. Mitteilung: Die Ursachen der Elektivität und Reifung des Dieudonné-Nährbodens. [**The Cause of the Selectivity and Ripening of Dieudonné Medium.**] II. Mitteilung: Neue Elektivnährböden für die Choleradiagnostik. [**New Selective Media for Cholera.**]—*Zent. f. Bakt.* I. Abt. Orig. 1932. Oct. 25 & Dec. 15. Vol. 126. Nos. 1/2 & 5/6. pp. 145–152. [14 refs.]; 450–455. [13 refs.]

The usefulness of the highly alkaline Dieudonné medium for the isolation of cholera vibrios from stools in more or less pure culture is a well established fact. Two theories, which may be described as the loss-of-ammonia and the action-of-carbon dioxide theories, have been invoked to account for the ripening of the medium. Three stages of transformation occur in Dieudonné medium, (1) of immaturity or unripeness, (2) of ripeness and selectivity for the cholera vibrio to the exclusion of other organisms and (3) of ripeness without selectivity, when *Bact. coli*, *Bact. faecalis alkaligenes* and other intestinal organisms will grow on the medium just as well as *V. cholerae*. It is probable, from the authors' experiments, that both the current theories accounting for ripening are to some extent true, with greater importance attributed to the carbon dioxide than to the ammonia theory, but that the entire explanation is one of attainment of a selective or non-selective pH upon exposure of the plate for a definite time to the air. Above pH 9·6 the plate is unsuitable for any growth: between 9·6 and 9 it is selective for *V. cholerae* and below 9 it is non-selective. *W. F. H.*

VEDDER (A.) & VAN DAM (W.). Nieuwe electieve voedingsbodems voor het Cholera-onderzoek. [**New Selective Media for Cholera.**]—*Nederl. Tijdschr. v. Hyg., Microbiol. en Serol.* 1932. Vol. 7. No. 3. pp. 197–205.

The chemical basis underlying the selectiveness and ripening of the well-known Dieudonné cholera medium depends on attainment of a

pH 9 to 9·6 [see above]. With this knowledge it became an easy matter to prepare media which possessed all the advantages and none of the disadvantages of the Dieudonné medium. They can be used immediately. These media are prepared as follows :—

No. 1.—(1) Boil for some minutes, haemoglobin 1 gm., N/5 KOH 20 cc. and obtain as much solution as possible. (2) Cool under the water tap. (3) Add 120 mgm. glycocol and 80 cc. of melted and cooled peptone agar (Witte peptone 1 gm.; sod. chloride ½ gm.; agar 3 gm.; water 100 cc.). (4) Pour plates. (5) Sow immediately without drying.

No. 2.—(1) Triturate 1 gm. haemoglobin with 4 cc. N/1 di-pot. carbonate (Anhydrous salt 6·9 gm.; boiled distilled water 100 cc.). (2) Add 1 cc. N/2 pot.-hydrogen carbonate solution (5 gm. per 100 cc. boiled distilled water) and 10 cc. distilled water. (3) Add 35 cc. peptone agar. (4) Pour plates.

Plates made from these media are immediately ripe and selective. They give abundant growths of *V. cholerae* and *V. El Tor*. Other organisms such as *Ps. pyocyanea, Bact. faecalis alkaligenes, Bact. coli* and enterococcus do not grow. *W. F. H.*

PASRICHA (C. L.), DE MONTE (A. J.) & GUPTA (S. K.). **Cholera and Cholera-like Vibriophages.**—*Indian Med. Gaz.* 1932. Sept. Vol. 67. No. 9. pp. 487–490. With 3 figs.

In a former publication (this *Bulletin*, 1932, p. 684) new types of phages D and E were reported and F was suggested. In this paper, which is on similar lines, the characters of phage E are described. It has the reciprocal action of the other four types, that is to say : "It can lyse the secondary growths of vibrios resistant to the other types of choleraphage and the secondary growth which develops after the action of type E on cholera vibrios is lysed by the other four types of choleraphage." Freshly isolated phage E had only very limited virulence for ultra-pure smooth vibrios. Of 50 strains of cholera vibrio tested against this phage only 4 were lysed. The number of strains, however, which were lysable was increased by adapting this type E to non-lysable strains and its virulence was easily raised by passage. It could only be obtained pure and separate from type A by serial passage on an ultra-pure rough vibrio on which type A cannot be propagated. Therapeutic choleraphage is improved by the addition of the new type.

Not only are pure-line types of choleraphage investigated by the authors but also the important group of cholera-like phages. Eight of these, active against vibrios which were non-agglutinable by cholera serum, non-lysable by choleraphage, were isolated. A classification of vibrios is put forward based on (1) their source from cholera stools, other stools and from water, (2) their agglutinability and (3) their lysability. This is admittedly an arbitrary classification, but helps to give precision to descriptions of changes which under selective conditions of growth may take place in a vibrio, such as the transformation from non-agglutinating to agglutinating or from phage-sensitive to phage-resistant. The series of choleraphages here considered is divisible into the type A and E which lyse only agglutinating cholera vibrios and the types B, C, D, which are capable, in addition, of lysing some strains of non-agglutinable vibrios. The reasoning is complicated, with this as one of the conclusions, that the true cholera vibrio does not die out when shed but loses its agglutinability and may be isolated from natural waters as a non-agglutinable vibrio Other conclusions have

reference to contamination of vibrios with phage, liberation of a symbiotic phage by the action of another powerful phage and to phages found in Nature being mutation forms of choleraphage types capable of reversion. *W. F. H.*

CHEN (W. K.). **Dissociation of** *V. cholerae* **by Bacteriophage.**—*Proc. Soc. Experim. Biol. & Med.* 1932. June. Vol. 29. No. 9. pp. 1160–1162. With 4 figs.

The technique used was to transfer 1cc. of an 18-hour peptone water culture to fresh peptone water to which 0·5 cc. bacteriophage had been added and incubate for one week. This process was repeated at weekly intervals and the culture plated out for examination of the resulting colonies. Variants appeared from among the phage-resistant secondary colonies after 2 to 4 weeks, 4 to 6 weeks and 6 to 10 weeks, which were motile-rough, non-motile-smooth and non-motile-rough colonies respectively. All these variants showed a tendency to reversion when grown in peptone water with transfer twice daily for 30 days and this reversion was still more rapid by animal passage.

W. F. H.

RAO (R. Sanjiva). **The Influence of H Ion Concentration on Cholera Bacteriophagy. A Preliminary Note.**—*Indian Jl. Med. Res.* 1932. Oct. Vol. 20. No. 2. pp. 377–385. With 16 plates.

Of the types into which bacteriophage has been divided, type A is quick acting and attacks only smooth cholera strains while types B and C are comparatively slow in action but dissolve both rough and smooth strains. According to the author, lysis by type A bacteriophage is enhanced within the optimum limits by increasing acidity and that of the type B by increased alkalinity. If there is no sharp line of demarcation between smooth and rough vibrios, it is understandable how an alteration of the pH of the medium in which they are grown may alter the grade of roughness of a vibrio and bring it into the category of one lysable by a subtype of A phage. In an alkaline medium the experiments given indicate that "cholera vibrios tend to arrange themselves in different groups according to their lysability by . . . the A type of cholera bacteriophage. It is then logical to presume that the different groups of cholera vibrios are only different grades of roughness." This is a very important conclusion and the author wisely remarks that further work is required to establish it.

W. F. H.

JUDE (René) & MILLISCHER (Pierre). Au sujet de la stérilisation des porteurs de vibrions cholériques par la voie buccale. [**Sterilization of Cholera Carriers Orally.**]—*C. R. Soc. Biol.* 1932. Oct. 21. Vol. 111. No. 31. pp. 263–264.

The authors describe their treatment of cholera carriers with vaccine in a dose of 5 to 6 cc. and concentration 5,000 million per cc. by the mouth as being probably more rapid in its effect than small doses of calomel. They desire that their results should be confirmed.

W. F. H.

HURI (Maurice). Essai de stérilisation des porteurs sains de vibrions cholériques par la méthode de Besredka. [**Sterilization of Healthy Cholera Carriers by Besredka's Method.**]—*C. R. Soc. Biol.* 1932. Dec. 16. Vol. 111. No. 39. pp. 877–878.

The development of automobile and air services across the desert of Damascus from Iraq has resulted in the arrival there of numerous carriers. Trials have been made at the quarantine station of the best methods to deal with such cases. The usual method had been to administer 0·20 gm. calomel at 48 hours interval and this took 3 to 5 days to effect sterilization. An account may be given of the first of three trials made: On the 11th September 13 cholera carriers out of 76 travellers were diagnosed by identification of the vibrios isolated, which were agglutinable to high titre with Pasteur Institute serum. Three of these received 10 cc. *per os* anticholera virus prepared from vibrios obtained from the Iraq epidemic. Another three received 10 cc. heated vaccine after preliminary ingestion of a capsule of bile; still another three received vaccine without bile, while four were kept as controls. All of those treated, whether with antivirus or vaccine were free of cholera vibrios in 24 hours, but agglutinable vibrios were present in the stools of all the controls. These four controls were now tested one by one and on successive days with antivirus, vaccine with bile and vaccine without bile, again with successful sterilization in 24 hours; the fourth control only still remained a carrier and was freed from vibrios finally by administration of antivirus. The sum total of carriers in the three trials was 74 and the results for these are the same as those recounted. *W. F. H.*

LEIVA (Lamberto). **Bactericidal Action of Di-Hydranol in Human Cholera Carriers.**—*Amer. Jl. Trop. Med.* 1932. Nov. Vol. 12. No. 6. pp. 509–512. With 2 figs.

Four daily successive negative examinations of stools after the last positive result are required before a carrier is allowed to be discharged. The number of cases available was 70 but two of these remained positive for over a month in spite of treatment and are excluded from consideration. Of the 68 remaining 32 received treatment with di-hydranol and 36 with salol-urotropin. For intervals of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 days between the last positive and the first negative examination, di-hydranol furnished 3, 9, 6, 5, 3, 0, 2, 1, 1, 1, 1 and salol-urotropin 6, 4, 10, 12, 3, 0, 0, 0, 1, 0, 0 cases respectively. The author considers that di-hydranol is a drug that is of service, ranking favourably with the salol-urotropin treatment in sterilizing cholera carriers. *W. F. H.*

KOROBKOVA (E.). Sur la cytologie du vibrion cholérique.—*Rev. Microbiol., Epidémiol. et Parasit.* 1931. Vol. 10. No. 4. pp. 335–342. With 37 figs. on 2 plates. [In Russian. French summary pp. 343–345.]

MEDICAL ZOOLOGY.

NYASALAND PROTECTORATE. **Medical Entomologist's Report for 1931** [LAMBORN (W. A.)].—*Nyasaland Protectorate Ann. Med. Rep. on Health & San. Condition for Year ending 31st December, 1931.* Appendix I. pp. 1–20.

This is a fine record of varied, purposeful, and prescient work.

1. *Tsetsefly Control.*—Steady improvement is reported in the Dowa and Fort Manning Districts of the Northern Province, where economic development by natives and Europeans of country formerly menaced by fly goes on apace, there being now 500 native tenants and extensive cultivation of tobacco and maize. Settlement is also going on along the trunk road, a large tract there being now a native reserve, and the number of Indian traders—indicative of prosperity—having increased to 200 ; the cultivation of tobacco is gradually leading to deforestation, and game is becoming scarce. Losses of stock south of the fly area certainly have occurred and have been said to be due to trypanosomiasis—a doubtful diagnosis. Experiment has shown that the flytraps found so useful against *Glossina pallidipes* in Zululand by HARRIS are of little value against *G. morsitans* which attacks its victims' flanks, nor did modifications of that trap improve matters.

2. *Research on the possibility of the transmission of trypanosomes (and other parasites) by carriers other than Glossina.*—Preparatory work in this direction has been fruitful in interesting and useful observations upon distribution, biology, and bionomy of various blood-sucking flies, the detail of much varied observation being tabulated in subject classifications that occupy 13½ foolscap pages. In the course of these investigations the author obtained a long series of egg-masses of *Tabanus biguttatus*, from most of which he bred out a minute parasitic Proctotrypid Hymenopter. He also succeeded in inducing this and eight other species of Tabanus to deposit their eggs in captivity, and thus obtained a volume of novel data on their bloodsucking habit in relation to reproduction. Eggs of *Haematopota decora* (which has a tapering abdomen) were observed to be planted well down in the ground. The author also succeeded in getting series of several species of Tabanus that had bitten animals (mostly cattle) carrying *Trypanosoma congolense* to feed on other healthy animals (dogs, white rats and a baboon) at intervals of 5 to 50 days afterwards. In exploring other possible ways for conveyance of that infection he introduced the excreta of such flies (passed while they were feeding on their bites) into the mouths of experimental animals—but without any result in 3 sets of experiments. And furthermore in a series of forty of such flies he examined microscopically smears from every region of the alimentary tract ; the smears for the most part were negative ; but (*a*) in the hindgut of a few of the flies swarms of organisms were found and were determined by Prof. J. Gordon THOMSON as Crithidia ; (*b*) in another instance " a flagellate with a truncated end like a Leptomonad ; and (*c*) in the proboscis of a Tabanus eleven small nematodes. Similar experiments were conducted with regard to possible conveyance of infection with *Trypanosoma congolense* by *Stomoxys calcitrans*—without positive result. Furthermore, in some preliminary and incomplete experiments the author satisfied himself that for experimentation such as is related above, Lyperosia could be kept alive up to 14 days and Haematopota is as amenable as Tabanus.

The author having observed that the larvae and puparia of *Tabanus africanus* on the Shire river are, like the larvae and pupae of Mansonioides, associated with the water-lettuce, *Pistia stratiotes*, tried whether this baneful plant could not be converted to beneficial uses—as it is in China and the Malay States—as food for pigs, and he found that two native pigs brought from the Angoni highlands consumed it readily once they had become accustomed to it. *A. Alcock.*

STABLER (Robert M.). **An Extended Study of Variations in a Single Race of a Coli-like Amoeba and its Bearing on the Specificity of** *Councilmania lafleuri.—Amer. Jl. Hyg.* 1932. July. Vol. 16. No. 1. pp. 1–31. With 7 text figs. & 24 figs. on 2 plates. [39 refs.]

The author has had under observation for 18 months a case of *Entamoeba coli* infection. In this case the amoeba has been exhaustively studied during the period, 507 stools having been examined and over 500 prepared slides and over 600 fresh mounts made. The main fact disclosed by this investigation is that the amoeba revealed all the morphological variations characteristic of both *Entamoeba coli* and *Councilmania lafleuri*. Buds and chromophile ridges supposed to be characteristic of *C. lafleuri* could be made to appear at will on the fixed and stained slides, the type and temperature of fixation being responsible for their production. For reasons given by the author there is no doubt that the case was infected with a pure strain of *Entamoeba coli*. On this account, as studies by other workers have already shown, the name *Councilmania lafleuri* may be correctly regarded as one of the many synonyms of *Entamoeba coli*. *C. M. Wenyon.*

SEGAL (Bess E.). **Budding and Other Variations in** *Endolimax nana*; **a Comparison with** *Councilmania tenuis* **Kofoid, 1928.**—*Amer. Jl. Hyg.* 1932. May. Vol. 15. No. 3. pp. 741–750. With 29 figs. on 2 plates. [10 refs.]

In 1917 KUENEN and SWELLENGREBEL described and figured two amoebae of the human intestine. These were *Entamoeba tenuis* and *Endolimax intestinalis*. It is generally assumed that the first of these was a small race of *Entamoeba histolytica* and the second *Endolimax nana*. KOFOID (1928) came to the conclusion that he had rediscovered *E. tenuis*, redescribed it and transferred it to his genus *Councilmania* as *C. tenuis* because he had observed bud formation through an opening in the cyst wall, a feature which is characteristic of the supposed genus. *C. tenuis*, however, as described by KOFOID does not resemble *E. tenuis* of KUENEN and SWELLENGREBEL, as KOFOID supposed, but rather their *E. intestinalis*, so that it seems not impossible that KOFOID confused some of the figures in KUENEN and SWELLENGREBEL'S plate illustrating their amoebae. Be that as it may, the author of the paper under review, who points out these discrepancies, has studied ten cases of *Endolimax nana* infection, fixing the parasites by a variety of techniques. After certain methods of fixation a varying percentage of the cysts show "budding," so that an amoeba corresponding with KOFOID'S *Councilmania tenuis* is produced. The "budding" is not a biological process but merely the result of damage to the cyst wall and the consequent protrusion of a bud of cytoplasm through the opening thus formed. The other features attributed to *C. tenuis* fall within the variations of

Endolimax nana so that the inevitable conclusion is reached that KOFOID's *Councilmania tenuis* not only is not KUENEN and SWELLENGREBEL's *Entamoeba tenuis* but merely *Endolimax nana*, the cysts of which have been damaged by faulty technique. *C. M. Wenyon.*

TATE (P.) & VINCENT (M.). **Susceptibility of English** *Culex pipiens* **L. to Infection with Bird Malaria.** [Correspondence.]—*Nature.* 1932. Oct. 22. Vol. 130. No. 328. p. 630.

In the course of experiments with 393 English *Culex pipiens* gorged on canaries heavily infected with bird malaria (*Plasmodium relictum*) 131 of the insects were dissected and 72 (55 per cent.) were found to be infected—oocysts and salivary glands. The infected insects readily transmitted the infection to healthy canaries. *A. A.*

PAINE (R. W.). **Coconut Committee. Entomological Report.**—*Ann. Bull. Div. Reps. Dept. Agric. Fiji 1931.* pp. 1–6. [Summarized in *Rev. Applied Entom.* 1932. Nov. Vol. 20. Ser. B. Pt. 11. p. 237.]

"A colony of *Megarhinus splendens*, Wied., the larvae of which attack those of certain other mosquitos in tree-hole water, barrels, etc., was introduced from Java into Fiji at the end of February. In Fiji it feeds principally on *Aëdes scutellaris*, Wlk. (*variegatus*, Dolesch.), the vector of filariasis. In one small area of swamp land containing trees (*Inocarpus edulis*) it became well established, causing a reduction of quite 50 per cent. in the numbers of *Aëdes*, but in other localities with a less concentrated supply of suitable breeding-places it has not been so successful. As oviposition does not occur on water on the ground, this mosquito cannot be expected to exercise any appreciable degree of control over *Culex* spp. or *A. vexans*, Mg."

HALL (W. W.) & VOGELSANG (W. A.). **Spider Poisoning : a Study of the Toxin of the Black Widow Spider** (*Latrodectus mactans*).—*U. S. Nav. Med. Bull.* 1932. Oct. Vol. 30. No. 4. pp. 471–478. With 4 figs. on 2 plates.

A good study of the effects of the bite of the (female) " black widow," the venomous Theridiid spider *Lathrodectus mactans*. It begins with summaries of two cases of bite, one of the thumb the other of the penis. The characteristics of the bite are (1) severe local pain, without any local inflammatory swelling, but afterwards spreading severely and widely with soreness and numbness or spasm and tetany, and (2) wherever the infliction of the bite may be, pain (often excruciating) and rigidity of the abdomen—a condition often simulating acute appendicitis or a ruptured gastric or duodenal ulcer. Macerated spiders injected *subcutim* into guineapigs gave negative results. Guineapigs bitten by a female spider usually flinched and squealed, the abdomen became tender and rigid, uncontrollable spasmodic movements of the legs began and increased in intensity, and were followed by noisy and difficult breathing, which in severe cases ended in pulmonary oedema. These symptoms began in from 1 to 5 minutes up to half-an-hour after the bite and ran their course in from 1 to 5 hours, after which the animal either succumbed or began to improve. During the second 24 hours painful movement (pseudoparalysis) was marked. Experimental animals dying within 5 hours showed only

pulmonary oedema; those bitten on the abdomen and succumbing after 48 to 72 hours showed patches of necrosis in liver, kidneys, spleen and adrenals. A single bite established complete immunity; subsequent bites caused no symptoms other than a local slough. But immune serum (antitoxin) protects only when given immediately after the bite; given later it does not seem to alter the ordinary course of reaction. The authors call the toxin "a non-haemolytic neurotoxin, which apparently acts on nerves and nerve-endings." [For earlier references to this and other species of the venomous genus *Lathrodectes* see this *Bulletin*, Vol. 19, pp. 497, 846; Vol. 20, p. 801; Vol. 21, p. 169; Vol. 23, p. 875; Vol. 24, pp. 401, 402, 895–897; Vol. 26, pp. 278, 779; Vol. 27, pp. 362, 935; Vol. 28, pp. 541, 542.] *A. A.*

DE ASIS (Cesareo). **The Bite of** *Latrodectus hasseltii*. [Correspondence.]—*Med. Jl. Australia.* 1932. Sept. 10. 19th Year. Vol. 2. No. 11. pp. 345–346.

The writer—from Cagayan in the Philippines—states that the venomous Theridiid spider *Latrodectus hasseltii* in the southern islands, as in Australia and New Zealand, is a species that commonly attacks man. The symptoms of its bite are profuse perspiration, high blood pressure, rapid and laboured respiration, slow pulse, numbness and weakness and paralysis of the lower limbs, and in some cases vomiting, chills, and dizziness. The alarming cases he treats with a 25 per cent. solution of $MgSO_4$ in 10 cc. doses *intravenim*, repeated as necessary. The spider, known in the Philippines as *aloy*, is a small black creature with a red back. *A. A.*

HASE (Albrecht). Ueber die unterschiedliche Widerstandsfähigkeit der parasitären Hauswanzen *Cimex lectularius* und *Cimex rotundatus* gegenüber der Einwirkung von Äthylenoxyd; nebst Bemerkungen üeber die Wirkung von Äthylenoxyd auf Meerschweine. [**On the Distinctive Resistance of the Parasitic Bedbugs** *Cimex lectularius* **and** *Cimex rotundatus* **to the Action of Ethylene-oxide; with Remarks on the Action of Ethylene-oxide on Guinea-pigs.**]—*Ztschr. f. Parasitenk.* 1932. Jan. 28. Vol. 4. No. 2. pp. 369–386. With 2 text figs. [7 refs.]

In all the series of experiments described in prodigious detail in this paper on the action of ethylene oxide (CH_2OCH_2) on bedbugs the concentration employed was 19·2 g./cbm. of ethylene oxide for 2–4 hours. From these experiments it appears that in the same concentration *C. rotundatus* is much more sensitive to ethylene oxide than *C. lectularius* and has a higher deathrate; that in all experiments certain larval stages of both species of Cimex were more resistant than adults of the same species, so that *C. lectularius* larvae are less sensitive than larvae of *C. rotundatus*; and that the eggs of *C. rotundatus* are less resistant than those of *C. lectularius*. Immediately after experimentation the bugs seemed to be unhurt; in the next 24 hours a large number of them seemed stupified, and after a further interval those so affected died. Neither *C. lectularius* nor *C. rotundatus* nor the eggs of either species are destroyed immediately by the 2–4 hours action of ethylene-oxide in the given concentration, but a high mortality occurring in both species after the 4 hours action seems to indicate the extreme limit of endurance.

For guineapigs the action of ethylene oxide in the same concentration for two hours was near the fatal limit and at four hours a great many were killed. *A. A.*

ITO (Y.). Dermatitis linearis und Dermatitis arteficialis durch den Extrakt von "Paederus idae Sharp." [**Dermatitis linearis and Dermatitis artificialis from the Extract of "Paederus idae Sharp."**] —*Fukuoka-Ikwadaigaku-Zasshi* (*Fukuoka Acta Med.*). 1932. Aug. Vol. 25. No. 8. [In Japanese. German summary pp. 60–61.]

Dermatitis linearis, common in Kyushu in summer, is probably identical with the dermatitis caused experimentally by the intra-cutaneous injection of the irritant secretion (or irritant extract) of the [Staphylinid beetle] *Paederus idae* Lewis *vel* Sharp, since the symptoms of the two are identical, namely a local inflammation beginning with hyperaemia, papules, and vesicles going on to pustules and then gradually subsiding and ending in a week or two in pigmentation. The irritant extract is soluble in alcohol, chloroform, and ether, but with difficulty in water or normal saline; it does not change in the course of ten months. *A. A.*

CHOPRA (R. N.) & CHOWHAN (J. S.). **Snake Venoms in Medicine.**—*Indian Med. Gaz.* 1932. Oct. Vol. 67. No. 10. pp. 574–578. [12 refs.]

The first part of this paper on Snake-venoms in Medicine takes four of the well-known Thanatophidia of the Oriental region from the natural history standpoint—their appearance, their geographical range, their venomous apparatus, and the physical, chemical, and pharmacological aspects of their venom. It is a good general presentation of current knowledge of *Naja tripudians*, *N. bungarus*, *Vipera russellii*, and *Echis carinatus*, and it need not detain us from the less formal and somewhat desultory final section headed "Therapeutic uses of the venom." Here we are informed that in India snake-venom is called *sarap vishi* in Hindi and *garala* in Sanskrit, that it is preserved for therapeutic use by drying or by rubbing with mustard oil and spreading on a plantain leaf, and that it is cobra venom that is chiefly used in the preparations of Indian physicians—in collapse, in cholera, in ascites, as an hepatic stimulant, and in small doses as a cardiac stimulant (although it is not absorbed from the gastro-intestinal tract or from other intact mucous membranes). In Mahomedan medicine cobra-blood is said to have a beneficial effect in leucoderma, and in Northern India a preparation of cobra and arsenic is a local application for syphilis. Turning to Western Medicine the authors note that rattlesnake venom has been much used in the treatment of pulmonary phthisis, acute pneumonia, chronic spasmodic cough, asthma, hoarseness, neuralgia, chorea, epilepsy, hystero-epilepsy, and haemophilia, and in other circumstances where a depressant action on nerve cells is desired. SPANGLER in Texas claimed that epilepsy could be cured by injections of snake-venom, since a few epileptics were so cured after rattlesnake bite; the same practitioner also used intramuscular injections of the protein of rattlesnake-venom (crotalin) for non-specific desensitization therapy in allergic asthma, taking the degree of eosinophilia produced as a guide to dosage and to frequency of administration. Cobra-venom is said to afford a means of

diagnosing malignant disease (Farmachidi's test), and venom of *Vipera aspis* to protect animals against the fixed virus of rabies (M. PHISALIX). There are Indians who habitually take small doses of snake-venom by the mouth [much after the method of Mithridates King of Pontus] with the idea of gaining immunity from poisons and diseases. The authors regard the use of cobra-venom by the mouth as baseless, and of rattle-snake-venom by injection, as a depressant of the central nervous system, as equally without justification. *A. A.*

ANDERSON (L. A. P.). **On the Standardization of Russell's Viper Antivenin.**—*Indian Jl. Med. Res.* 1932. July. Vol. 20. No. 1. pp. 1–24.

As is stated in the Introduction, the standard Kasauli antiserum is prepared from the mixed venoms of the cobra and the daboia (Russell's viper) and is active against both ; and in the routine standardization of the Kasauli antivenin before issue only the neutralizing value against cobra venom is estimated. In the present paper methods of standardizing antidaboia serum by means of its neutralizing power *in vitro* and *in vivo* are described.

In the investigation of the minimum lethal dose of daboia venom, upon which standardization is based, earlier workers had noticed with regard to this venom, not only that individual samples appear to vary in their toxic effect but also that manifestations of toxic reaction, which appear chiefly in the vascular system, vary according to the dose and the route by which it is administered, causing on the one hand thrombosis and on the other hand haemorrhages. Thus LAMB and HANNA here quoted, state that when a dose that just fails to cause death from intravascular thrombosis is given intravenously the animal presents only very slight symptoms or none at all ; and in the author's own experiments on the neutralization of test-doses of daboia venom injected into muscles, either the death of the animal occurred almost immediately or no symptoms were observed. The uncertainties and irregularities that may follow intramuscular injection preclude this method from experimental determination of the minimum lethal dose, and for standardization of daboia antivenom—though not for estimation of its therapeutic value—it is necessary that in all tests both antivenom and venom must be injected intravenously so as to meet rapidly in the bloodstream.

The following are the author's conclusions :—

" (1) Methods of standardizing anti-daboia serum, by means of its neutralizing power *in vitro* and *in vivo* have been described and the results of experiments given.

" (2) The *in vitro* method, by reason of the ease with which it can be carried out and the regularity of the results obtained, appears to be more suitable for routine work and is considered to provide a reliable method of standardizing a serum against daboia venom.

" (3) The results of these tests are not to be interpreted as directly related to the quantity of daboia venom which will be effectively neutralized by serum used therapeutically in cases of snake-bite, but only as indicating a standard which may be used to prevent the issue of serum of poor value.

" (4) It is suggested that anti-daboia serum of such a potency that 1 cc. will neutralize *in vitro* at least 1·5 mg. daboia venom is suitable for issue.

" (5) For any biological method of standardizing antivenin against daboia venom all injections, both of serum or venom, or mixtures of both, should be given directly into the blood stream.

"(6) Evidence is put forward that the choice of animal for use in such standardizing tests is important, the suitability of the animal probably increasing with the proximity of the site of injection to the heart and great vessels, and the relative size of the vein used for inoculation. It is suggested that the pigeon fulfils these conditions better than other animals hitherto used.

"(7) The M.L.D. of daboia venom on which standardization is based should be the smallest dose which when injected intravenously brings about rapid death by intravascular clotting.

"(8) Daboia venoms appear to vary considerably in their constitution and consequently in their toxic effect, and the sample before use should be carefully tested for its effect when administered intravenously. Only those samples are suitable for standardization tests which on intravenous injection cause rapid death by intravascular thrombosis, and whose minimum lethal dose intravenously is readily determined and is not subject to fluctuation. Certain samples are definitely unsuitable for standardization work.

"Further investigation is required to determine the nature and cause of this variable action of daboia venoms." *A. A.*

MAITRA (G. C.) & MALLICK (S. M. K.). **Observations on Detoxication of Daboia Venom by Hepatic Lipoids with a Note on the Anti-Viperine Potency of Kasauli Antivenin.**—*Indian Jl. Med. Res.* 1932. July. Vol. 20. No. 1. pp. 327–334. With 1 plate.

At the Kasauli Research Institute the necrotic action of Russell's viper venom has always been a trouble in the routine immunization of horses for antivenin requirements. The authors briefly discuss some methods of treating viper venom so as to abate this virulence without affecting its immunizing property and they describe in full detail how in pursuance of VELLARD's method they prepared and obtained from sheep's liver the alcohol and ether-soluble extractives—here called hepatic lipoids—which lessened the necrotic action of Russell's viper venom without impairing its immunizing value. Before exposing the said venom to the action of these lipoids it was dissolved in normal saline and mixed with glycerine (3 gm. to 1 gm. of venom); the mixture was evaporated to a jelly; to this was added 5 gm. of lipoids, and the combination was incubated in a stoppered weighing-bottle for 2 months at 37°C. The venom thus detoxified was found sterile at the end of the 2 months. The authors further describe in detail how the venom when detoxified was tested on six guineapigs, two of which received gradually increasing weekly injections of untreated viper venom, the other four similarly receiving weekly injections of *treated* venom of the same brew. The two that received untreated venom showed local necrosis and pus-formation with 0·3 mgm., whereas the four that received up to 3·0 mgm. of *treated* venom showed no local necrosis, although in some cases a simple swelling occurred the day after the injection. To determine whether the treated (detoxified) viper venom could produce specific antibodies (in combination with cobra venom as in the immunization of horses for the practical purpose of Kasauli) two young goats received cobra venom and treated Russell's viper venom in gradually increasing weekly injections for a term of six months. "It was gratifying to note the absence of local necrotic reaction throughout the immunization period." When the serum of both of the goats was found to be sufficiently potent the animals were bled and antivenin was collected; 1 cc. of serum from each goat neutralized 0·5 mgm. of cobra venom and 0·8 mgm. of Russell viper venom when tested on

pigeons. An "antivenin horse" known to be very sensitive to the action of viper venom and notorious for developing abscesses, showed great reduction of these inflammatory local reactions after the preliminary treatment of the viper venom with hepatic lipoids.

From these studies it would appear that hepatic lipoids when allowed to remain in contact with daboia [Russell's viper] venom for a year at 37°C. do certainly reduce its necrotic action on animal tissues. In horses there was complete absence of local reaction to smaller doses, and though when the immunizing dose was increased to 60 mgm. a certain amount of necrosis was noticed it was remarkably less than in the reaction produced by untreated daboia venom. Simple local swelling sometimes seen after injection of treated venom the authors attribute to the presence of protein particles; but they think that if, as VELLARD holds, the detoxication of viperine venom be due to the lecithin abundant in liver tissue it might be worth while to try the effect of pure commercial lecithin on daboia venom. Besides confirming the detoxifying effect, without interference with immunizing power, of hepatic lipoids on daboia venom, a biological test of ascertaining the antiviperine potency of antivenins is described and the minimum antiviperine potency of Kasauli antivenin is explained and recorded as 1 mgm. of daboia venom per cc. of serum for standard pigeons, death appearing to be due to the action of the venom on the medullary centres, not to thrombosis. *A. A.*

EPSTEIN (David). **The Effects of Toad Venom on the Eye.**—*South African Med. Jl.* 1932. June 25. Vol. 6. No. 12. pp. 403–404.

Reports of a case of temporary painful blindness in a man into whose eye an African leopard-toad (*Bufo regularis*) had squirted some of its parotoid venom from a distance of two feet, and of appropriate experiments made on a cat with the venom. The blindness is due to local irritation, dilatation of the pupil (with subsequent anaesthesia of the cornea) and consequent interference with accommodation; the irritation and subsequent anaesthesia being due to the presence of a digitalis-like substance and the dilatation of the pupil being due to the presence of adrenalin in the venom. *A. A.*

MILLER (David). The Biology and Economic Status of New Zealand Muscidae and Calliphoridae.—Part I. Historical Review.—*Bull. Entom. Res.* 1932. Dec. Vol. 23. Pt. 4. pp. 469–476. [41 refs.]

PEARSE (A. S.). Ecology of the Ectoparasites of Nigerian Rodents and Insectivores.—Reprinted from *Jl. Mammalogy.* 1929. Aug. Vol. 10. No. 3. pp. 229–239. [18 refs.]

YAWS AND SYPHILIS.

BLACKLOCK (D. B.). **Yaws and Syphilis.**—*Ann. Trop. Med. & Parasit.* 1932. Oct. 29. Vol. 26. No. 3. pp. 423–455. [41 refs.]

The object of this paper is to re-examine those points which some writers have elaborated as differential criteria between yaws and syphilis. The author passes in review these diagnostic points as they are to be found in the vast majority of textbooks.

Yaws.—Not congenital; primary sore extragenital; typical yaw pathognomonic; furfuraceous and plantar lesions characteristic; mucous membranes not affected; itching common; alopecia not known; eyes unaffected; visceral lesions absent; nervous system never seriously affected; no endothelial proliferation; better resisted; constitutional disturbances slight; does not respond to mercury.

Syphilis.—Congenital; primary sore usually genital; syphilis seldom imitates framboesia; mucous membranes affected; itching rare; alopecia may occur; iritis common, choroiditis and retinitis rare; visceral lesions occur, *i.e.*, pericellular cirrhosis, gumma of liver, etc.; nervous system prone to infection, tabes, G.P.I.; endarteritis obliterans of viscera, cerebral thrombosis; attacks constitution affecting vital structures; responds well to mercury.

Arguments are adduced under these several headings in an attempt to show where reasoning has been fallacious in the past. Here is the author's summary :—

" (1) An attempt has been made to approach the yaws and syphilis controversy without prejudice, a notoriously difficult matter.

" (2) The usually accepted differential criteria have been discussed and examined from various aspects.

" (3) It is shown that in compiling the differential tables, fallacies have been introduced chiefly owing to comparisons being made between things which are not properly comparable.

" (4) Arguments are brought forward against comparing yaws, which is mainly a non-venereal disease of children in rural areas of the tropics and which begins by an extragenital primary lesion, with venereal adult syphilis of Europeans.

" (5) The accounts of adult venereal syphilis as it affects natives in tropical countries, are not as yet complete, but so far as they go they indicate that such syphilis varies as greatly, in many respects, from venereal syphilis in adults in temperate climates, as does yaws.

" (6) The evidence that yaws is other than syphilis modified by age, race and various local conditions, does not appear convincing; the onus of proof rests on those who maintain that these are two distinct diseases."

[This is a most interesting contribution to the discussion. It remains to be seen whether Professor Blacklock's arguments will make a general appeal. They will require careful consideration Since the author considers " the onus of proof rests on those who maintain that these are two distinct diseases," it is presumed that he is convinced of their identity.] *H. S. Stannus.*

VON BÜLOW (T.). Un cas de surinfection dans le pian. [**Surinfection in Yaws.**]—*Bull. Soc. Path. Exot.* 1932. Oct. 12. Vol. 25. No. 8. pp. 869–874.

The author starts by pointing out the necessity of distinguishing between " surinfection " and reinfection. He then goes on to define the two conditions but both under the name of surinfection, doubtless

as the result of a printer's error, so that the reader is left in doubt as to what the author is trying to prove.

The case which forms the basis of the article was a woman aged 20 in Costa Rica. In 1925 she had a primary yaw, according to her story, on the front of the lower part of the leg followed by two or three very small secondary lesions, all of which disappeared 18 months later without treatment. In 1929 a primary yaw [*sic*] appeared on the foot, followed by secondary lesions which disappeared quickly while the primary lesion persisted. The author concludes that this was a case of "surinfection" made possible by the poor immunity developed in the first attack owing to the lack of a good outcrop of secondary lesions.

H. S. S.

MONTEL (R.). A propos de la communication de T. von Bulow sur un cas de surinfection dans le pian. [**Von Bulow's Paper on Surinfection in Yaws.**]—*Bull. Soc. Path. Exot.* 1932. Nov. 9. Vol. 25. No. 9. pp. 946–947.

Montel criticizes the deductions made by VON BULOW in his case which he called one of surinfection in yaws. He points out that the history of the first infection is not conclusive and the so-called second infection might well be a late ulcerative lesion. Montel holds in contradistinction to VON BULOW that the primary lesion seldom undergoes spontaneous healing, but lasts a long time, though very easily cured by N.A.B.

[This criticism appears well merited. Much that is written upon yaws is recorded without sufficient care.] *H. S. S.*

DE AZEVEDO (Rinaldo). A aurotherapia na bouba. [**Gold Treatment of Yaws.**]—*Brasil-Medico.* 1932. Nov. 19. Vol. 46. No. 47. pp. 984–987. With 1 fig.

The author gives details of four cases of yaws in patients of 13, 14, 18 and 35 years. He treated them by means of solganal B. To the oldest he gave 0·1 gm. intravenously at 5-day intervals for 6 doses; the next (18 years of age) had the same amount for 3 doses, similarly administered, followed by 0·15 gm. intramuscularly for 3 doses at the same intervals; the two youngest had the latter method only. The lesions cleared rapidly in all cases, leaving of course some scarring, but none showed any signs of intolerance and in none did the total amount exceed 0·9 gm. A fifth patient is referred to, but his history is not given, beyond the fact that he was a man of "30 odd" years who was cured with a series of 8 intravenous injections of 0·1 gm. each at five-day intervals. *H. H. S.*

TESSITORE (C.). Néosalvarsan e rhodarsan nella cura del pian e della sifilide infantile per via endomuscolare. [**Neosalvarsan and Rhodarsan in Young Children with Yaws or Syphilis.**]—*Arch. Ital. Sci. Med. Colon.* 1932. Oct. 1. Vol. 13. No. 10. pp. 633–634. English summary (5 lines).

In the Belgian Congo both neosalvarsan and rhodarsan have been used by gluteal injection in strengths of 1–1·5 per cent. [amount injected is not mentioned], for yaws or syphilis in children of 2 years or less. Within a short period the parents returned with their infants and those who had received rhodarsan presented local infiltration, painful, rapidly spreading, doughy and threatening to suppurate; they had also a raised temperature.

These signs began to appear within 12–24 hours of the injection. Neo-salvarsan gave rise to a slight local, but no systemic reaction. For this reason instructions have been sent to medical officers to employ the latter drug for all young children requiring arsenical injections. *H. H. S.*

FRÖHLICH (Hans). Zur Kenntnis der luetischen juxtaartikulären Knotenbildungen. [**J.A.N. due to Syphilis.**]—*Arch. f. Dermat. u. Syph.* 1932. Aug. 13. Vol. 166. No. 1. pp. 226–233. With 6 figs.

Judging by the fact that five cases of J.A.N. have been recorded in the Breslau skin clinic in the last nine years as "etiology unknown," the author believes that it is still not generally recognized that this affection is a syphilitic one. Notes of two cases are given, both men, both without venereal history, but both with manifestations of syphilis and positive W.R. In each some response to anti-specific treatment was noted. *H. S. S.*

STEEL (C. R.). The Aetiology of Yaws.—*Jl. Trop. Med. & Hyg.* 1932. Nov. 1. Vol. 35. No. 21. pp. 321–324. With 12 figs. & 3 charts.

VERBUNT (J. A.). Over den gewonen vorm van den uitslag bij framboesia.—*Nederl. Tijdschr. v. Geneesk.* 1932. Nov. 26. Vol. 76. No. 48. pp. 5418–5425. With 5 figs. on 2 plates.

REVIEWS AND NOTICES.

SMITH (E. C.) [B.A., M.D. (Dublin), D.P.H., D.T.M. & H. (Eng.), etc.]. **An Atlas of Skin Diseases in the Tropics.**—pp. x+60. With 2 coloured plates & 253 figs. on 100 plates. 1932. London: John Bale, Sons & Danielsson, Ltd., 83–91, Great Titchfield Street, W.1. [21s.]

This volume may be described as a very meritorious effort to fill a serious gap in medicine. Its scope is restricted to West Africa, however, a fact which is fully explained both in the folder and in the preface, and is determined by the very excellent reason that the book is based on purely personal experience, which fact greatly increases its value. Nevertheless it would perhaps be better to indicate this restriction in the title. A few other criticisms may be made, but they are all of small importance and are tendered as being suggestive of ways in which some improvement might possibly occur. As both the subject matter and the figures are arranged alphabetically, the omission of an index might be justified, but it would be useful where different synonyms are in common use. The only exception to this alphabetical arrangement is the inclusion of Gangosa after Yaws and it seems rather a pity to spoil the system when it is not absolutely proven that the disease is a late form of Yaws. Again, on glancing through the table of contents it would appear that Tinea cruris is not illustrated, yet fig. 116 shows an excellent example. The subject matter is presented in a very readable manner. The paper and printing are alike both excellent and clear, giving rise to no eye-strain.

The book is essentially an atlas, yet in spite of that many of the diseases could be dealt with a little more fully with advantage. Dermal Leishmaniasis is dismissed with the remark that it is not seen in Southern Nigeria, yet it is of such importance that it would be justifiable to omit the personal element here. In the description of Epidermophytosis, no reference is made to infection of the feet or hands. In Moniliasis, paronychia is neglected. Also approval cannot be extended to the paragraph on Molluscum contagiosum for it is by no means always easy to diagnose, nor is the following phrase correct, " if incised a lobulated mass of fat or sebaceous material is obtained," unless it is clearly indicated that this is a purely clinical description. Nor is " shirt-button tumour " a happy phrase, for it is liable to cause confusion with Biskra button, and is certainly not a good clinical description of a " domed " tumour. To the useful details concerning the microscopical methods of detecting fungi, there might be added a warning against the common error of diagnosing fat globules as spores.

The photographs are deserving of the highest praise. Rarely has such a clear and typical collection been seen. Of the whole 250 or more, only five are unworthy of their company. The illustration of Onychomycosis is good but does not show the effects of friability or the thickening of the nail-bed sufficiently ; one of Tinea flava could be excluded as there are other and better examples ; Herpes zoster of the popliteal space might be almost any vesicular eruption ; the Haemangioma of the scalp is badly out of focus, whilst the " Monilial patches on face of young girl " are quite indistinguishable. Although this list of complaints might seem formidable, they are in reality only small and almost unnoticeable in a book of this description. To its general presentation only the highest praise can be given, and it is to be sincerely hoped that the author will be sufficiently encouraged to produce a larger edition in due course. He has set an example which could be imitated by workers in other tropical fields, with great advantage to the whole of dermatology. *M. Sydney Thomson.*

CHOYCE (C. C.) [C.M.G., C.B.E., B.Sc., M.D., F.R.C.S., Professor of Surgery, Univ. of London, etc.] & BEATTIE (J. Martin) [M. A., M.D., C.M., M.R.C.S., Professor of Bacteriology, Univ. of Liverpool, etc.]. (Pathological Editor.) [Edited by.] **A System of Surgery.** Third Edition. In Three Volumes. Vol. 1. pp. xxiv +1112. With 33 colour & 67 half-tone plates & 285 figs. in text. Vol. 2. pp. xv+1111. With 16 colour & 11 half-tone plates & 367 figs. in text. Vol. 3. pp. xvi+1107. With 11 colour & 39 half-tone plates & 277 figs. in text. 1932. London, Toronto, Melbourne & Sydney: Cassell & Company, Ltd. [£6 net the 3 volumes.]

The Third Edition of Choyce's System of Surgery contains a large amount of new matter necessitated by the surgical advances of the nine years which have elapsed since the publication of the second edition. 29 new plates and 210 new illustrations have been introduced and there are fourteen new contributors.

Volume I deals with "Surgical Pathology, Tumours, Venereal Diseases, Breast and General Surgery." This list does not, however, do justice to its contents and requires some amplification. There is a particularly instructive chapter on the preparation, administration and mode of action of serums and vaccines with due note of anaphylaxis and an interesting short reference to Bacteriophage. The Elastoplast treatment of chronic leg ulcers and various forms of skin grafting are briefly described. General surgical technique, the tannic acid treatment of burns and scalds, haemorrhage and shock are all ably discussed. A short chapter deals in a succinct manner with Toxaemia, Septicaemia and Pyaemia while another chapter, copiously illustrated by skiagram reproductions, treats of X-ray diagnosis in all its many branches. Other chapters deal with Radium Therapy, Tuberculosis, Gonorrhoea and Syphilis. The beautifully reproduced coloured plates of syphilitic lesions of skin and mucous membrane and the useful tables of routine treatment of various types of case deserve special mention. Some 250 pages are devoted to an exhaustive classification and description of Tumours.

Yaws, Gangosa, Tropical Sore, Leprosy, Madeira Foot and Ulcerating Granuloma have short sections devoted to them which have been brought up-to-date by the addition of notes of recently introduced developments chiefly in treatment. In conditions such as these, in which active research is still in progress, it is perhaps unavoidable that a certain lack of conviction should be suggested by the multiplicity of the medicaments recommended for treatment.

Sections on Glanders, Actinomycosis, Tetanus, Anthrax, Schistosomiasis, Elephantiasis, Bites and Stings by insects and snakes and even Poison Wounds inflicted by fish indicate how the needs of surgeons in all parts of the world have been catered for.

The four pages devoted to Plastic Surgery, which are included in the chapter on Lesions of the Skin and Subcutaneous Tissue, give no indication of the great advances which have been made in this branch of Surgery during recent years. We feel that the inclusion of a few well-chosen diagrams and photographic illustrations, while not materially adding to the length of the chapter, would be appreciated by the many surgeons who are called upon to carry out the less complicated plastic procedures in the course of their routine work.

The chapter on Breast, which completes the volume, is a masterly exposition of the subject.

Volume II.

The chapter on the spleen will be found valuable chiefly for its able discussion of the various forms of Splenomegaly and the indications for Splenectomy.

In the chapter on Malformations of the Face, Lips and Palate, we are glad to note the addition of much new material and several new illustrations, and we are particularly pleased to see due notice given in the section on Cleft Palate to the work of VEAU of Paris and WARDILL of Newcastle, for we consider that the methods developed by these two surgeons represent the main advances made in recent years in this difficult branch of surgery.

The short section on Dysenteric Ulceration of the intestine makes no reference to the two distinct varieties of the disease, Bacillary (bacterial) and Amoebic. Although the bulk of the section, and more particularly the treatment described, applies to the former type, the statement that " abscess of the liver is also a frequent complication " could apply only to the latter. In a later chapter by another contributor, it is correctly stated that liver abscess " only very occasionally complicates the bacterial form of the disease."

Assuming that the section refers to bacillary dysenteric ulceration, we find ourselves opposed to the suggestion of making an artificial anus in the ascending colon, for it is common experience to find the caecum and ascending colon seriously involved and in severe cases, in spite of the recognized objections to an artificial anus in the small bowel, we believe that nothing short of an ileostomy holds out any real prospect of cure. Ileo-sigmoidostomy is recommended as preferable, when possible, to the formation of an artificial anus. This procedure, although certainly offering rest to the most seriously affected parts of the bowel, provides no means of active treatment of the ulcerated areas. In the majority of cases involvement of the lower parts of the colon renders it impracticable. When performed it is essential that efficient medication of the short-circuited loop of actively ulcerated bowel shall be provided for by the concomitant establishment of caecostomy or appendicostomy.

The section on Subphrenic Abscess is an excellent guide to the differential diagnosis of suppurative conditions in, or in the neighbourhood of, the liver.

Diseases of the rectum and anus are fully discussed and the treatment of piles by sclerosing injections and of fissure-in-ano by local anaesthetic injections is briefly described.

The section on Tropical Abscess of the Liver cannot be allowed to pass without the following criticisms. No mention is made, in the discussion of diagnosis, of lateral X-rays in which irregularity of outline frequently indicates the presence of an abscess when little evidence is given by the more usual antero-posterior views. The treatment of secondarily infected abscess by the Carrel-Dakin method, which has proved so efficacious, is omitted. A 3 inch exploring needle appears to us much too short an instrument for effectively exploring so large a mass of tissue as an enlarged right lobe of the liver.

The description of renal function tests and of the routine investigation of urinary conditions is well worthy of special study.

Volume III.

Much new material has been introduced by the new contributor of the chapter on " The Neck " more particularly in that section dealing with diseases of the Thyroid Gland.

The article on Peripheral Nerves has been brought up-to-date and is greatly helped by the inclusion of new diagrams. Due mention is made of recent developments in the surgery of the sympathetic nervous system, and we note with interest that Periarterial Sympathectomy is condemned as a procedure founded on an erroneous conception of the distribution of sympathetic nerve supply to limb vessels.

The chapters on Skull, Brain and Spinal Cord have been revised and remain the outstanding contribution to the literature of the subjects they treat.

There are excellent chapters on Bone and Joint diseases and Orthopaedic Surgery. The latter contains an instructive section on physiological and mechanical principles of Bone grafting and an equally interesting one on

Manipulative Surgery. From the latter may be re-quoted, in reference to joint stiffness, the rule " When in doubt, move " as being likely to give more successes than failures.

The first edition of Choyce's System of Surgery has been for many years our favourite book of surgical reference. We therefore commenced this review of the new edition with a very definite bias in its favour ; our study of the 3,000 odd pages has served only to confirm this bias for it is difficult to imagine a publication more replete with information presented in so readable a form. The time has passed when any one surgeon could be expected to know enough about every branch of Surgery to make his writings on subjects outside his specialty in any sense authoritative. The pages of these three volumes speak with the recognized authority of the specialists who have undertaken the writing of chapters on subjects of which they have extensive first-hand knowledge and the " scissors and paste " method of compilation plays no part in their production.

The volumes are not intended as a text book for students but they should be found on the book-shelves of all practising surgeons who wish to keep themselves abreast of recent advances and should make a special appeal to those working for the higher examinations in surgery.

T. Pomfret Kilner.

WONG (K. Chimin) [L.M.S., Hongkong] & WU LIEN-TEH [M.A., M.D. (Cantab.), etc.]. **History of Chinese Medicine. Being a Chronicle of Medical Happenings in China from Ancient Times to the Present Period.**—pp. xviii + 706. With frontispiece, 92 illustrations & 1 coloured map (in pocket). 1932. Tientsin: Tientsin Press, Ltd. [30s.].

It is probable that most of us who take up this volume will do so in a spirit of mild literary interest with little thought of acquiring useful medical knowledge. Its pages, however, unfold a remarkable story reaching back to the very foundations of history and covering the whole range of Chinese medical history—a matter of over 4,500 years. The plan of this work is to consider both the old style Chinese medical practice (the time-honoured indigenous art) and the introduction and development of Western Medicine to China. The earliest records are those of the Ancient or Legendary Period (2697–1122 B.C.) which was largely mythological and full of legends concerning the founders of Chinese medicine, the most venerated of whom was SHEN NUNG, The Father of Medicine, still worshipped by native Drug Guilds as their patron god. In course of time these legends developed into more reliable history and we come to the second great phase, the Historical or Golden Period (1122 B.C.–960 A.D.), when, under the CHOU Dynasty, literature, art and philosophy flourished—a state of civilization.

In 206 B.C. was founded the HAN Dynasty which is regarded as the most glorious epoch in Chinese medical history, and was rendered specially memorable from the fact that during this period there lived three of the greatest doctors China has ever had who placed Medicine on a scientific basis that has stood the test of time curiously well. And all this, be it noted, at a time when our ancestors in Britain were savages and cave-dwellers. The march of progress was, however, interrupted during the succeeding T'ANG Dynasty when owing to Indian influence the cure of disease fell under a system of charms, incantations and magic. Briefly stated the CHOU Dynasty was the age of philosophy, the HAN Dynasty the age of science and the T'ANG Dynasty the age of superstition. From the tenth to the seventeenth century Chinese medical thought became confused and controversial: this was the Mediaeval Period (961–1800 A.D.). It was succeeded by the Modern or Transitional Period (1801–1932 A.D.) which has had as its most prominent feature the struggle for supremacy between the old and new forces, the latter slowly and steadily gaining ground.

The foregoing observations summarize the salient features of Chinese medical history. The first three periods, as dealt with in this book, are written by Dr. CHIMIN WONG who is regarded in the East as the leading medical historian of China. Chapter VI is specially interesting as it introduces to the Western reader the Nei Ching, Internal Classics or Canon of Medicine, which is the oldest as well as the greatest Chinese medical classic. It is a compilation by various writers made 3,000 years ago and sums up the experimental, physiological and theoretical knowledge of all the preceding centuries. It is the earliest attempt to systematize the medical thoughts of these ancient times and even at the present day it is the favourite theme of Chinese medical writers to annotate and comment on this work. Among other interesting items it shows that at this early period the ancient Chinese had indeed grasped a good part of the truth concerning the circulation of the blood.

They were a sapient lot these old Chinese doctors. In the Record of Rites written during Confucian times (552–479 B.C.) we note a warning that no one should take medicine compounded by a doctor who was not backed up by an experience of three generations. Also we are told that if a medicine does not raise a commotion in the patient the disease will not be cured by it, and that one can remove the trouble only when one knows the cause. In the opinion of WEN CHUNG TZU the able doctor should first attend to sleep and diet before resorting to drugs.

Chapter VIII gives an enlightening account of Drs. TS'ANG, CHANG and HUA who lived between the years 180 B.C.–270 A.D. The fame of the last of the trio, Dr. HUA, rests chiefly on his marvellous skill as a surgeon. He successfully trephined for brain tumours and introduced the operation of castration to produce eunuchs for the Imperial Palace. By means of an effervescing powder he induced anaestheisa though this was no novelty, for in 200 B.C. it is noted that P'IEN CH'IAO had procured numbness and insensibility by a narcotic wine. There are other notices of the life and works of leaders of Chinese medical men a-down the Ages, and a good description is given of the PEN TS'AO or Chinese Materia Medica which has a history as old as that of the Chinese race and has gone through many editions, the first of which is ascribed to SHEN NUNG who lived 2838–2693 B.C. Few departments of our profession escaped the notice of these wonderful ancients. Public Health, Obstetrics, Gynaecology, Surgery were all handled in a surprisingly scientific way that will grip the attention not only of our medical historians but of general readers who will find much of interest in Dr. WONG's account.

Latter day history beginning in 1804 saw the first seeds of modern health and medicine planted by medical missionaries in China. It is dealt with by Dr. WU LIEN TEH who has given as full an account as he could gather of the work of Foreign and Chinese doctors in establishing modern scientific medicine in China. It is a record of slow progress till within the past thirty years when the profession has made its influence more widely felt especially in the realm of Public Health. But this story lacks the fascination of the traffics and discoveries of ancient times.

The printing and illustration of the volume are a credit to the Tientsin Press Ltd. of Tientsin, North China. *Douglas Gray.*

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